10/534,660>05/04/2007

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(FILE 'HOME' ENTERED AT 21:09:42 ON 04 APR 2007)

FILE 'HCAPLUS' ENTERED AT 21:11:03 ON 04 APR 2007
E HORWITZ M/AU 25
L1 115 S (E3 OR E4 OR E13 OR E14)
L2 413135 S SULFO?
L3 6 S L1 AND L2

FILE 'REGISTRY' ENTERED AT 21:12:38 ON 04 APR 2007
L4 1 S 7732-18-5/RN
L5 1 S 74-93-1/RN
L6 1 S 143-33-9/RN
L7 1 S 1066-33-7/RN
L8 1 S 1629-58-9/RN
L9 1 S 5925-75-7/RN
L10 1 S 26628-22-8/RN
L11 1 S 66735-71-5/RN
L12 1 S 1982-67-8/RN
L13 1 S 15985-39-4/RN
L14 1 S 66735-67-9/RN
L15 1 S 66735-68-0/RN
L16 1 S 9023-70-5/RN
L17 13 S L4-L16

FILE 'HCAPLUS' ENTERED AT 21:16:45 ON 04 APR 2007
L18 419072 S L17
L19 5 S L18 AND L3

FILE 'STNGUIDE' ENTERED AT 21:17:32 ON 04 APR 2007

FILE 'HCAPLUS' ENTERED AT 21:23:07 ON 04 APR 2007
E "66735-67-9"/BI,RN 25
L20 6 S E3 OR E5 OR E6 OR E7
L21 5 S L20 NOT L19

FILE 'STNGUIDE' ENTERED AT 21:24:42 ON 04 APR 2007

FILE 'REGISTRY' ENTERED AT 21:26:35 ON 04 APR 2007
L22 STR 15985-39-4
L23 2 S L22 FAM SAM

FILE 'STNGUIDE' ENTERED AT 21:26:53 ON 04 APR 2007

FILE 'REGISTRY' ENTERED AT 21:33:49 ON 04 APR 2007
L24 STRUCTURE UPLOADED
L25 50 S L24 SSS SAM

FILE 'STNGUIDE' ENTERED AT 21:34:48 ON 04 APR 2007

FILE 'REGISTRY' ENTERED AT 21:36:15 ON 04 APR 2007
L26 STRUCTURE UPLOADED
L27 50 S L26 SSS SAM

FILE 'REGISTRY' ENTERED AT 21:43:05 ON 04 APR 2007
L28 STRUCTURE UPLOADED
L29 30 S L28 SSS SAM

FILE 'STNGUIDE' ENTERED AT 21:45:29 ON 04 APR 2007

FILE 'REGISTRY' ENTERED AT 21:46:20 ON 04 APR 2007
L30 STRUCTURE UPLOADED

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L31             3 S L30 SSS SAM
L32            35 S L30 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 21:47:29 ON 04 APR 2007
L33            68 S L32
L34            62 S L33 AND 1800<=PY<=2002

     FILE 'STNGUIDE' ENTERED AT 21:48:56 ON 04 APR 2007

     FILE 'HCAPLUS' ENTERED AT 21:50:19 ON 04 APR 2007
L35         39032 S MYCOBACTER?
L36             1 S L33 AND L35

=> s ?bacter?
L37        775618 ?BACTER?

=> s l33 and l37
L38             3 L33 AND L37

=> s l38 not l36
L39             2 L38 NOT L36
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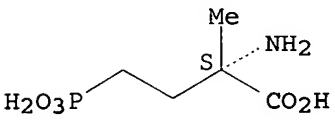
L34 ANSWER 1 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:504345 HCAPLUS
DOCUMENT NUMBER: 140:22628
TITLE: Design and synthesis of conformationally constrained analogs of l-2-amino-4-phosphonobutanoic acid (l-ap4) and l-2-amino-2-methyl-4- phosphonobutanoic acid (map4) as metabotropic glutamate receptor ligands
AUTHOR(S): Prabhu, Sarika Vidyanand
CORPORATE SOURCE: Univ. of Minnesota, Minneapolis, MN, USA
SOURCE: (2002) 149 pp. Avail.: UMI, Order No. DA3066383
From: Diss. Abstr. Int., B 2003, 63(10), 4619
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT 157381-42-5DP, analogs
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design and synthesis of conformationally constrained analogs of l-2-amino-4-phosphonobutanoic acid and l-2-amino-2-methyl-4-phosphonobutanoic acid as metabotropic glutamate receptor ligands)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



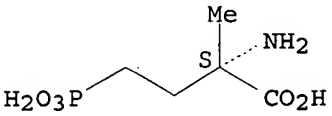
L34 ANSWER 2 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:670544 HCAPLUS
DOCUMENT NUMBER: 137:363255
TITLE: Closure of the venus flytrap module of mGlu8 receptor and the activation process: Insights from mutations converting antagonists into agonists
AUTHOR(S): Bessis, Anne-Sophie; Rondard, Philippe; Gaven, Florence; Brabet, Isabelle; Triballeau, Nicolas; Prezeau, Laurent; Acher, Francine; Pin, Jean-Philippe
CORPORATE SOURCE: Department de Chimie et Biochimie Pharmacologiques et Toxicologiques, Unite Mixte de Recherche 8601-Centre National de la Recherche Scientifique, Universite Rene Descartes-Paris V, Paris, 75270/06, Fr.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(17), 11097-11102
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ca2+, pheromones, sweet taste compds., and the main neurotransmitters glutamate and γ-aminobutyric acid activate G protein-coupled receptors (GPCRs) that constitute the GPCR family 3. These receptors are dimers, and each subunit has a large extracellular domain called a Venus flytrap module (VFTM), where agonists bind. This module is connected to a heptahelical domain that activates G proteins. Recently, the structure of the dimer of mGlu 1 VFTMs revealed two important conformational changes resulting from glutamate binding. First, agonists can stabilize a closed state of at least one VFTM in the dimer. Second, the relative orientation of the two VFTMs in the dimer is different in the presence of glutamate,

such that their C-terminal ends (which are connected to the G protein-activating heptahelical domain) become closer by more than 20 Å. This latter change in orientation has been proposed to play a key role in receptor activation. To elucidate the resp. role of VFTM closure and the change in orientation of the VFTMs in family 3 GPCR activation, we analyzed the mechanism of action of the mGlu8 receptor antagonists ACPT-II and MAP4. Mol. modeling studies suggest that these two compds. prevent the closure of the mGlu8 VFTM because of ionic and steric hindrance, resp. We show here that the replacement of the residues responsible for these hindrances (Asp-309 and Tyr-227, resp.) by Ala allows ACPT-II or MAP4 to fully activate the receptors. These data are consistent with the requirement of the VFTM closure for family 3 GPCR activation.

IT 157381-42-5
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(mGlu8 receptor antagonist; closure of venus flytrap module of mGlu8 receptor and the activation process and insights from mutations converting antagonists into agonists)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

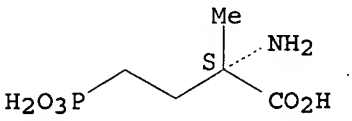
L34 ANSWER 3 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:530853 HCAPLUS
DOCUMENT NUMBER: 138:130580
TITLE: A new binding mode of competitive antagonists to metabotropic glutamate receptors exemplified by the mGluR1-receptor antagonist AIDA (RS-aminoidan-1,5-dicarboxylic acid)
AUTHOR(S): Belenikin, M. S.; Baskin, I. I.; Palyulin, V. A.; Zefirov, N. S.
CORPORATE SOURCE: Moscow State University, Moscow, 119992, Russia
SOURCE: Doklady Biochemistry and Biophysics (2002), 384, 131-135
CODEN: DBBOAL; ISSN: 1607-6729
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using a group I antagonist, the positions of antagonists in the interlobar space of the metabotropic glutamate receptors were evaluated. Mol. dynamics (MD) calcns. were carried out using the exptl. determined amino terminal domain structures of the open mGluR1 form. RS-Aminoindan-1,5-dicarboxylic acid (AIDA), a competitive antagonist of group I metabotropic glutamate receptors, served as a ligand. Based on the MD calcns., the most preferable position occupied by an antagonist of the subgroup I metabotropic glutamate receptor, AIDA, in the interlobar space is the position on the surface of the agonist-binding lobe, which is similar to that of agonists. This indicated that an alternative positioning of competitive antagonists is possible in the ligand-binding centers of metabotropic glutamate receptors.

IT 157381-42-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(new binding mode of competitive antagonists to metabotropic glutamate

receptors exemplified by the mGluR1-receptor antagonist AIDA (RS-aminoidandicarboxylic acid))
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

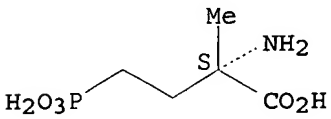
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

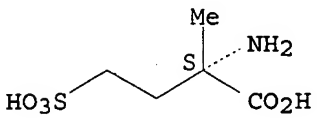
L34 ANSWER 4 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:925011 HCAPLUS
DOCUMENT NUMBER: 136:318765
TITLE: Pharmacophore identification and bioactivity prediction for group I metabotropic glutamate receptor agonists by the electron-conformational QSAR method
AUTHOR(S): Rosines, Eran; Bersuker, Isaac B.; Boggs, James E.
CORPORATE SOURCE: Institute for Theoretical Chemistry, Department of Chemistry and Biochemistry, The University of Texas at Austin, Austin, TX, 78712, USA
SOURCE: Quantitative Structure-Activity Relationships (2001), 20(4), 327-334
CODEN: QSARDI; ISSN: 0931-8771
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pharmacophore for group I metabotropic glutamate receptor (mGluR1) agonists is revealed and their activity predicted by means of the previously developed and further improved electron-conformational (EC) method. A distinguishing feature of this method is that in addition to revealing the pharmacophore of activity as a set of specific atomic electronic features arranged in a special geometry, it allows for prediction of the activity quant. as a function of the parameters of pharmacophore flexibility and anti-pharmacophore shielding groups. Conformational anal., electronic structure calcns., and matrix processing are performed for the training set of 29 compds., 13 active and 16 inactive, and the pharmacophore of mGluR1 agonists is evaluated. It contains a four-point skeleton of three oxygen atoms and one nitrogen atom at certain interat. distances with restricted atomic interaction indexes whereby all these parameters are determined within certain tolerances. The pharmacophore parameter flexibilities, as well as the influence of the anti-pharmacophore shielding and other auxiliary groups are parameterized and weighted by seven consts., their values being obtained from a least-square regression with very good statistics: R2 = 0.97, F = 589 (.apprx.100% level of confidence), and a standard error of about 5% of the range of measured values. The results are also tested with the leave-one-out cross validation method that yields prediction statistics R2 = 0.91. The E statistics were also evaluated illustrating the role of each of the activity parameters involved.
IT 157381-42-5 171228-34-5
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(pharmacophore identification and bioactivity prediction for group I metabotropic glutamate receptor agonists by electron-conformational QSAR method)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171228-34-5 HCAPLUS
CN L-Isovaline, 4-sulfo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 5 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:833023 HCAPLUS
DOCUMENT NUMBER: 135:376738
TITLE: Compounds and methods for modulating cerebral amyloid angiopathy using inhibitors of an amyloid β peptide
INVENTOR(S): Green, Allan M.; Gervais, Francine
PATENT ASSIGNEE(S): Neurochem, Inc., Can.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085093	A2	20011115	WO 2000-IB2078	20001222 <--
WO 2001085093	A3	20020829		
WO 2001085093	A9	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2395314	A1	20011115	CA 2000-2395314	20001222 <--
AU 2001084313	A5	20011120	AU 2001-84313	20001222 <--
EP 1251837	A2	20021030	EP 2000-993855	20001222 <--
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BR 2000016652	A	20021119	BR 2000-16652	20001222 <--
US 2003003141	A1	20030102	US 2000-747408	20001222
US 6670399	B2	20031230		
JP 2003532656	T	20031105	JP 2001-581748	20001222
AU 2006201445	A1	20060504	AU 2006-201445	20060406
PRIORITY APPLN. INFO.:			US 1999-171877P P	19991223

AU 2001-84313 A3 20001222
WO 2000-IB2078 W 20001222

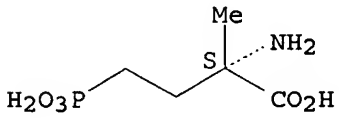
OTHER SOURCE(S): MARPAT 135:376738

AB The invention provides methods of inhibiting cerebral amyloid angiopathy (CAA) and treating a disease state characterized by cerebral amyloid angiopathy, e.g., Alzheimer's disease, in a subject using an inhibitor of the 39-40 amino acid amyloid β peptide (Aβ40). The Aβ40 inhibitor is selected from, e.g., sulfonic acid derivs., such as ethanesulfonic acid, 1,2-ethanedisulfonic acid, 1-propanesulfonic acid, 1,3-propanedisulfonic acid, 1,4-butanedisulfonic acid, 1,5-pentanedisulfonic acid, 2-aminoethanesulfonic acid, 4-hydroxy-1-butanesulfonic acid, 1-butanesulfonic acid, 1-decanesulfonic acid, 2-propanesulfonic acid, 3-pentanesulfonic acid, 4-heptanesulfonic acid, etc., and pharmaceutically acceptable salts thereof or from from phosphonic acid derivs., such as diethylphosphonoacetic acid, phenylphosphonic acid, 3-aminopropylphosphonic acid, propylphosphonic acid, etc. The compds. are formulated in a dispersion system, a liposome formulation, or microspheres using a polymeric matrix. The polymeric matrix is selected from natural polymers, such as albumin, alginate, cellulose derivs., collagen, fibrin, gelatin, and polysaccharides, or synthetic polymers such as polyesters, polyethylene glycol, poloxamers, and polyanhydrides. For example, the ability of compds. of the invention to inhibit CAA was measured in 9 wk old hAPP transgenic mice treated with two different concns. of a compound of the present invention, 3-amino-1-propanesulfonic acid sodium salt, 100 and 30 mg/kg. Mice were administered the compound for 8 wk, after which they were sacrificed and their brains were perfused and processed for histol. staining with Thioflavin S. This method may also be used as a screening method for determining activity of a candidate compound for inhibiting CAA. The extent of CAA in brain sections obtained from these animals was qual. determined following staining. The results indicate that the test compound was effective in (i) reducing the number of mice showing CAA, and (ii) showing an effect on the severity of the deposition seen in the brain vasculature of these animals.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of amyloid β peptide for modulating cerebral amyloid angiopathy)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 6 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:537258 HCAPLUS
DOCUMENT NUMBER: 135:352635
TITLE: Anticonvulsant activity of a mGlu4α receptor selective agonist, (1S,3R,4S)-1-aminocyclopentane-1,2,4-tricarboxylic acid
AUTHOR(S): Chapman, A. G.; Talebi, A.; Yip, P. K.; Meldrum, B. S.
CORPORATE SOURCE: Institute of Psychiatry, Department of Neurology, King's College London, De Crespigny Park, London, SE5 8AF, UK
SOURCE: European Journal of Pharmacology (2001),

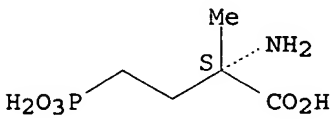
424(2), 107-113
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The metabotropic Group III agonist, (1S,3R,4S)-1-aminocyclopentane-1,2,4-tricarboxylic acid (ACPT-1), selective for the mGlu4α receptor, suppresses sound-induced seizures in DBA/2 mice following its intracerebroventricular (i.c.v.) administration (ED50 5.6 [2.9-10.7], nmol i.c.v., 15 min, clonic phase) and in genetically epilepsy-prone (GEP) rats following focal administration into the inferior colliculus (ED50 0.08 [0.01-0.50], nmol, 60 min, clonic phase). ACPT-1 also protects against clonic seizures induced in DBA/2 mice by the Group I agonist, (RS)-3,5-dihydroxyphenylglycine (3,5-DHPG) (ED50 0.60 [0.29-1.2], nmol i.c.v.) and by the Group III antagonist, (RS)-α-methylserine-O-phosphate (MSOP) (ED50 49.3 [37.9-64.1], nmol i.c.v.). Another Group III agonist, (RS)-4-phosphonophenyl-glycine (PPG), preferentially activating the mGlu8 receptor, previously shown to protect against sound-induced seizures in DBA/2 mice and GEP rats, also protects against seizures induced in DBA/2 by 3,5-DHPG (ED50 3.7 [2.4-5.7], nmol i.c.v.) and by the Group III antagonist, MSOP (ED50 40.2 [21.0-77.0], nmol i.c.v.). At very high doses (500 nmol i.c.v. and above), Group III antagonists have pro-convulsant and convulsant activity. The anticonvulsant protection against sound-induced seizures in DBA/2 mice provided by a fully protective dose (20 nmol, i.c.v.) of the mGlu4 receptor agonist ACPT-1, is partially reversed by the co-administration of the Group III antagonists, MSOP, (RS)-α-methyl-4-phosphonophenylglycine (MPPG) or (S)-2-amino-2-methyl-4-phosphonobutanoic acid (MAP4), in the 20-50 nmol dose range. At doses of 50-200 nmol, MPPG and MAP4 cause further reversal of the ACPT-1 anticonvulsant protection, while the MSOP effect on ACPT-1 protection is abolished at higher doses. In contrast, the anticonvulsant protection against sound-induced seizures in DBA/2 mice provided by a fully protective dose (20 nmol, i.c.v.) of the mGlu8 receptor agonist PPG, is not significantly affected by the co-administration of the same Group III antagonists, MSOP, MPPG or MAP4. We conclude that activation of either mGlu4α or mGlu8 receptors confer anticonvulsant protection in DBA/2 mice. Furthermore, the metabotropic Group III receptor antagonists, MSOP, MPPG, and MAP4 appear to be functionally selective for the mGlu4 receptor in this system.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(anticonvulsant activity of a mGlu4α receptor selective agonist, (1S,3R,4S)-1-aminocyclopentane-1,2,4-tricarboxylic acid)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 7 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:97735 HCAPLUS
DOCUMENT NUMBER: 135:55950
TITLE: (S)-3,4-DCPG, a potent and selective mGlu8a receptor agonist, activates metabotropic glutamate receptors on

primary afferent terminals in the neonatal rat spinal cord

AUTHOR(S): Thomas, N. K.; Wright, R. A.; Howson, P. A.; Kingston, A. E.; Schoepp, D. D.; Jane, D. E.

CORPORATE SOURCE: School of Medical Sciences, Department of Pharmacology, University of Bristol, Bristol, BS8 1TD, UK

SOURCE: Neuropharmacology (2001), 40(3), 311-318
CODEN: NEPHBW; ISSN: 0028-3908

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

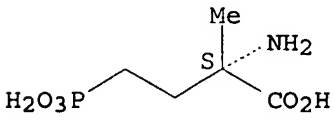
AB (S)-3,4-Dicarboxyphenylglycine (DCPG) has been tested on cloned human mGlu1-8 receptors individually expressed in AV12-664 cells co-expressing a rat glutamate/aspartate transporter and shown to be a potent and selective mGlu8a receptor agonist (EC50 value 31±2 nM, n=3) with weaker effects on the other cloned mGlu receptors (EC50 or IC50 values >3.5 μM on mGlu1-7). Electrophysiol. characterization on the neonatal rat spinal cord preparation revealed that (S)-3,4-DCPG depressed the fast component of the dorsal root-evoked ventral root potential (fDR-VRP) giving a biphasic concentration-response curve showing EC50 values of 1.3±0.2 μM (n=17) and 391±81 μM (n=17) for the higher and lower affinity components, resp. The receptor mediating the high-affinity component was antagonized by 200 μM (S)-α-methyl-2-amino-4-phosphonobutyrate (MAP4, KD value 5.4±1.5 μM (n=3)), a group III metabotropic glutamate (mGlu) receptor antagonist. The α-Me substituted analog of (S)-3,4-DCPG, (RS)-3,4-MDCPG (100 μM), antagonized the effects of (S)-3,4-DCPG (KD value 5.0±0.4 μM, n=3) in a similar manner to MAP4. (S)-3,4-DCPG-induced depressions of the fDR-VRP in the low-affinity range of the concentration-response curve were potentiated by 200 μM (S)-α-ethylglutamate (EGLU), a group II mGlu receptor antagonist, and were relatively unaffected by MAP4 (200 μM). However, depressions of the fDR-VRP mediated by the AMPA selective antagonist (R)-3,4-DCPG were not potentiated by EGLU, suggesting that the low-affinity component of the concentration-response curve for (S)-3,4-DCPG is not due to antagonism of postsynaptic AMPA receptors. It is suggested that the receptor responsible for mediating the high-affinity component is mGlu8. The receptor responsible for mediating the low-affinity effect of (S)-3,4-DCPG has yet to be identified but it is unlikely to be one of the known mGlu receptors present on primary afferent terminals or an ionotropic glutamate receptor of the AMPA or NMDA subtype.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
((S)-3,4-DCPG, a potent and selective mGlu8a receptor agonist, activates metabotropic glutamate receptors on primary afferent terminals in neonatal rat spinal cord)

RN 157381-42-5 HCAPLUS

CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

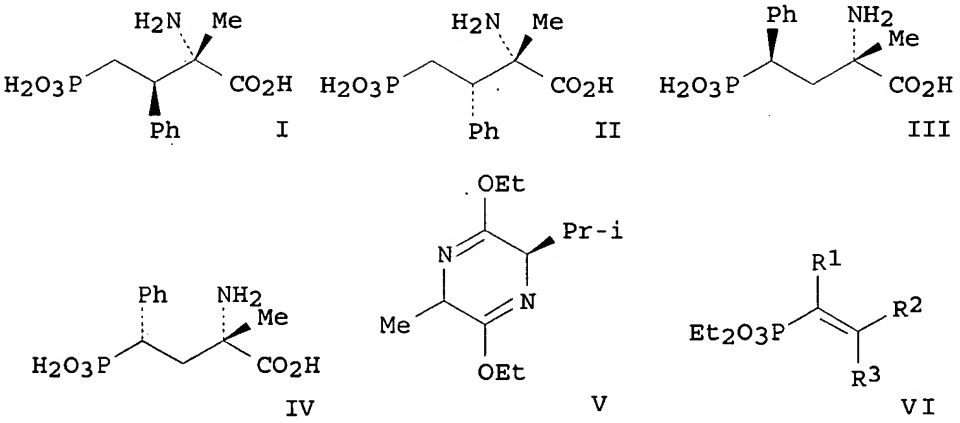


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 8 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:55592 HCAPLUS

DOCUMENT NUMBER: 134:193694
TITLE: Stereoselective synthesis of 2-amino-2-methyl-4-phosphonobutanoic acid derivatives (MAP4 analogs)
AUTHOR(S): Ruiz, Maria; Ojea, Vicente; Fernandez, M. Carmen; Conde, Susana; Diaz, Aniana; Quintela, Jose M.
CORPORATE SOURCE: Departamento de Quimica Fundamental e Industrial, Facultade de Ciencias, Universidade da Coruna, Coruna, 15071, Spain
SOURCE: Proceedings of ECSOC-1: The First International Electronic Conference on Synthetic Organic Chemistry; [and] Proceedings of ECSOC-2: The Second International Electronic Conference on Synthetic Organic Chemistry, Sept. 1-30, 1997, 1998 (1999), Meeting Date 1997-1998, 398-401. Editor(s): Lin, Shu-Kun; Pombo-Villar, Esteban. Molecular Diversity Preservation International: Basel, Switz. CODEN: 69ASBO
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:193694
GI

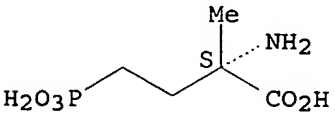


AB Electronic conference proceedings on the diastereoselective synthesis of several derivs. of MAP4 [H2O3PCH2CH2C(Me)(NH2)CO2H] were presented. For example, MAP4 derivs. I-IV were prepared The synthesis strategy involved the conjugate addition of the lithium salt of bislactim ether V to alkenylphosphonates VI (R1 = R3 = H, R2 = Ph; R1 = R2 = H, R3 = Ph; R2 = R3 = H, R1 = Ph). The resulting adducts were treated to vigorous acid hydrolysis to give I-IV.

IT 157381-42-5DP, derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of phenyl-substituted (amino)(methyl)phosphonobutanoic acids)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

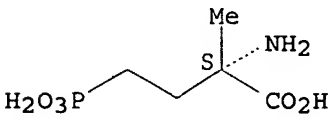
L34 ANSWER 9 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:256024 HCAPLUS
DOCUMENT NUMBER: 133:13023
TITLE: Pharmacological characterization of the rat metabotropic glutamate receptor type 8a revealed strong similarities and slight differences with the type 4a receptor
AUTHOR(S): De Colle, C.; Bessis, A.-S.; Bockaert, J.; Acher, F.; Pin, J.-P.
CORPORATE SOURCE: Centre INSERM-CNRS de Pharmacologie-Endocrinologie, UPR 9023-CNRS, Montpellier, 34094, Fr.
SOURCE: European Journal of Pharmacology (2000), 394(1), 17-26
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the brain, group-III metabotropic glutamate (mGlu) receptors mGlu4, mGlu7 and mGlu8 receptors play a critical role in controlling the release process at many glutamatergic synapses. The pharmacol. profile of mGlu4 receptor has been studied extensively, allowing us to propose a pharmacophore model for this receptor subtype. Surprisingly, the activity of only a few compds. have been reported on mGlu7 and mGlu8 receptors. In order to identify new possibilities for the design of selective compds. able to discriminate between the members of the group-III mGlu receptors, we have undertaken a complete pharmacol. characterization of mGlu8 receptor and compared it with that of mGlu4 receptor, using the same expression system, and the same read out. The activities of 32 different mols. revealed that these two mGlu receptors subtypes share a similar pharmacol. profile. Only small differences were noticed in addition to that previously reported with S-carboxyglutamate (S-Gla) being a partial agonist at mGlu4 receptor and a full antagonist at mGlu8 receptor. These include: a slightly higher relative potency of the agonists 1S,3R and 1S,3S-aminocyclopentane-1,3-dicarboxylic acid (ACPD), S-4-carboxyphenylglycine (S-4CPG) and S-4-carboxy-3-hydroxyphenylglycine (S-4C3HPG), and a slightly higher potency of the antagonists LY 354740 and RS-α-methyl-4-phosphonophenylglycine (MPPG) on mGlu8 receptor. When superimposed on the mGlu4 receptor pharmacophore model, these mols. revealed three regions that may be different between the ligand binding sites of mGlu8 and mGlu4 receptors.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(rat metabotropic glutamate receptor type 8a pharmacol. characterization and comparison with mGluR4a and pharmacophore models therefor)

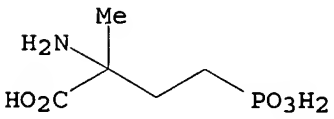
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 10 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:236781 HCAPLUS
DOCUMENT NUMBER: 133:69122
TITLE: Conservation of the ligand recognition site of metabotropic glutamate receptors during evolution
AUTHOR(S): Parmentier, M.-L.; Galvez, T.; Acher, F.; Peyre, B.; Pellicciari, R.; Grau, Y.; Bockaert, J.; Pin, J.-P.
CORPORATE SOURCE: Centre INSERM-CNRS de Pharmacologie-Endocrinologie, UPR 9023-CNRS, Montpellier, 34094, Fr.
SOURCE: Neuropharmacology (2000), 39(7), 1119-1131
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mammalian metabotropic glutamate receptors (mGluRs) are classified into 3 groups based on their sequence similarity and ligand recognition selectivity. Recently, we identified a Drosophila mGluR (DmGluAR) which is about equidistant, phylogenetically, from the 3 mGluR groups. However, both the G-protein coupling selectivity and the pharmacol. profile of DmGluAR, as analyzed with mutated G-proteins and a few compds., look similar to those of mammalian group-II mGluRs. In the present study we carefully examined the pharmacol. profile of DmGluAR, and compared it to those of the rat mGlu1a, mGlu2 and mGlu4a receptors, representative of group-I, II and III resp. The pharmacol. profile of DmGluAR was found to be similar to that of mGlu2R, and only very small differences could be identified at the level of their pharmacophore models. These data strongly suggest that the binding sites of these two receptors are similar. To further document this idea, a 3D model of the mGlu2 binding domain was constructed based on the low sequence similarity with periplasmic amino acid binding proteins, and was used to identify the residues that possibly constitute the ligand recognition pocket. Interestingly, this putative binding pocket was found to be very well conserved between DmGluAR and the mammalian group-II receptors. These data indicate that there has been a strong selective pressure during evolution to maintain the ligand recognition selectivity of mGluRs.
IT 78405-44-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(metabotropic glutamate receptors ligand-binding site conservation during evolution)
RN 78405-44-4 HCAPLUS
CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:173870 HCAPLUS
DOCUMENT NUMBER: 132:318216
TITLE: Constraints on proper folding of the amino terminal domains of group iii metabotropic glutamate receptors
AUTHOR(S): Peltekova, V.; Han, G.; Soleymanlou, N.; Hampson, D. R.
CORPORATE SOURCE: Faculty of Pharmacy and Department of Pharmacology, University of Toronto, Toronto, ON, Can.
SOURCE: Molecular Brain Research (2000), 76(1),

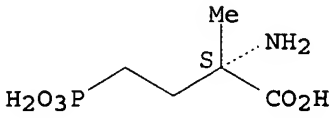
180-190
CODEN: MBREE4; ISSN: 0169-328X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The glutamate binding site of the G-protein coupled metabotropic glutamate receptors (mGluRs) is contained within the large extracellular N-terminal domain (ATD) of the receptor. In this study, the authors examined the ligand binding properties and cellular dispositions of the membrane-bound mGluR4 and mGluR8 subtypes of mGluRs, and a series of truncated versions of these receptors. Truncation of the ATDs of mGluR4 and mGluR8 40 amino acids upstream of the first transmembrane domain produced soluble proteins that were secreted into the cell culture media of transfected human embryonic kidney cells. The soluble receptors retained ligand binding capabilities. Addnl. constructs of the ATDs of mGluR4 and mGluR8 were assessed for their ability to bind the agonist [3H]L-AP4 and for secretion from cells. A shorter mGluR4 construct truncated 98 amino acids upstream from the first transmembrane domain failed to bind [3H]L-AP4, while the analogous mGluR8 construct displayed a low level of binding. Unlike the full-length receptors, which were expressed on the cell surface, or the soluble constructs which were secreted, the shorter constructs were primarily associated with intracellular membranes. These observations suggest that the cysteine-rich region may be important for efficient secretion, but not absolutely obligatory for ligand binding. Surprisingly, longer constructs encoding the entire ATDs of mGluR4 and mGluR8 failed to bind ligand and were localized intracellularly. Together, these findings demonstrate that there are strict limitations on the proper folding of truncated versions of the ATDs of mGluR4 and mGluR8. Specifically, all of the leucine-isoleucine-valine binding protein homol. region, and part of the cysteine-rich region is required for optimal secretion in a soluble form that retains ligand binding activity.

IT 157381-42-5
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(constraints on proper folding of amino terminal domains of group III metabotropic glutamate receptors)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

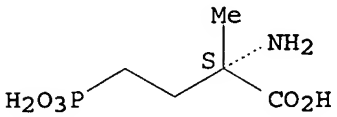


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 12 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:117282 HCAPLUS
DOCUMENT NUMBER: 132:132273
TITLE: (+)-MCPG blocks induction of LTP in CA1 of rat hippocampus via agonist action at an mGluR group II receptor. [Erratum to document cited in CA128:317182]
AUTHOR(S): Breakwell, N. A.; Rowan, M. J.; Anwyl, R.
CORPORATE SOURCE: Dep. Physiology Trinity College, Univ. Dublin, Dublin, Ire.
SOURCE: Journal of Neurophysiology (1999), 82(5), 12
CODEN: JONEA4; ISSN: 0022-3077
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal

LANGUAGE: English
AB The electrophysiol. traces in Figs. 2A and 5A are incorrect because of inadequate labeling of the stored traces in the computer files that were used to prepare the figures. The corrected versions of Figs. 2A and 5A are given. The corrections do not significantly affect the quant. results or alter the conclusions of the article.
IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
((+)-MCPG blocks induction of LTP in CA1 of rat hippocampus via agonist action at an mGluR group II receptor (Erratum))
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

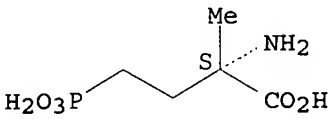
Absolute stereochemistry. Rotation (+).



L34 ANSWER 13 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:31061 HCAPLUS
DOCUMENT NUMBER: 132:246238
TITLE: Role of metabotropic glutamate receptor subclasses in modulation of adenylyl cyclase activity by a nootropic NS-105
AUTHOR(S): Hirouchi, Masaaki; Oka, Michiko; Itoh, Yoshinori; Ukai, Yojiro; Kimura, Kiyoshi
CORPORATE SOURCE: Nippon Shinyaku, Research Laboratories, Kyoto, 601-8550, Japan
SOURCE: European Journal of Pharmacology (2000), 387(1), 9-17
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The involvement of metabotropic glutamate (mGlu) receptors in the modulatory actions of a novel cognition enhancer, (+)-5-oxo-d-prolinepiperidinamide monohydrate (NS-105), on adenylyl cyclase activity in rat cerebrocortical membranes and primary neuronal cultures was investigated using selective antagonists and antisense oligodeoxynucleotides for mGlu receptor subclasses. In rat cerebrocortical membranes, the inhibitory action of NS-105 (0.1 μM) on forskolin-stimulated cAMP formation was blocked by a group II mGlu receptor antagonist, (±)-α-ethylglutamic acid, and by a group III antagonist, (+)-2-amino-2-methyl-4-phosphonobutanoic acid (MAP-4), but not by a group I antagonist, (±)-1-aminoindan-1,5-dicarboxylic acid (AIDA), whereas the facilitation of cAMP formation by NS-105 (1 μM) in pertussis toxin-pretreated membranes was abolished by AIDA but not by (±)-α-ethylglutamic acid or MAP-4. In primary cultured neurons of mouse cerebral cortex, the inhibitory action of NS-105 on adenylyl cyclase activity disappeared after treatment with antisense oligodeoxynucleotides for group II (mGlu2 and mGlu3 receptors) and group III (mGlu4 and mGlu7 receptors) but not group I (mGlu5 receptor) mGlu receptor subclasses. These findings suggest that the inhibitory action of NS-105 on adenylyl cyclase activity is mediated through group II and group III mGlu receptor subclasses while the facilitatory action is dependent on the group I mGlu receptor subclass.
IT 157381-42-5, (+)-2-Amino-2-methyl-4-phosphonobutanoic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)
(metabotropic glutamate receptor subclass role in modulation of adenylyl cyclase activity by nootropic NS-105)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

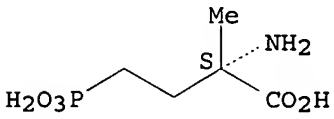
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

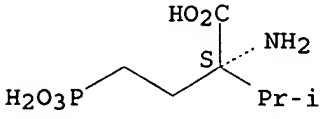
L34 ANSWER 14 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:30387 HCAPLUS
DOCUMENT NUMBER: 132:151895
TITLE: Synthesis of α-substituted aminocarboxylic acids
AUTHOR(S): Saratovskikh, I. V.; Kalashnikov, V. V.; Ragulin, V. V.
CORPORATE SOURCE: Institute of Physiologically Active Substances, Russian Academy of Sciences, Chernogolovka, Russia
SOURCE: Russian Journal of General Chemistry (Translation of Zhurnal Obshchei Khimii) (1999), 69(7), 1173-1175
CODEN: RJGCEK; ISSN: 1070-3632
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alkylation of Schiff bases of amino acids, PhCH:NCHRCO2R1 (R = Me, Ph, Me2CH, PhCH2; R1 = Me, Et) with R22P(O)(CH2)nBr (R2 = OEt, Ph; n = 2-5) followed by hydrolysis gave 32-85% 7 R32P(O)(CH2)nCR(NH2)CO2H (R3 = OH, Ph; R = same as above; n = 2-5).
IT 157381-42-5P 258284-99-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of phosphorylalkyl substituted amino acids)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 258284-99-0 HCAPLUS
CN L-Valine, 2-(2-phosphonoethyl)- (9CI) (CA INDEX NAME)

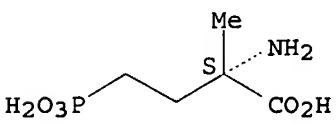
Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 15 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:721664 HCAPLUS
DOCUMENT NUMBER: 132:48186
TITLE: Effect of the umami peptides on the ligand binding and function of rat mGlu4a receptor might implicate this receptor in the monosodium glutamate taste transduction
AUTHOR(S): Monastyrskaia, Katherine; Lundstrom, Kenneth; Plahl, Doris; Acuna, Gonzalo; Schweitzer, Christophe; Malherbe, Pari; Mutel, Vincent
CORPORATE SOURCE: Pharma Division Preclinical CNS Research Hoffmann-La Roche Ltd., Basel, CH-4070, Switz.
SOURCE: British Journal of Pharmacology (1999), 128(5), 1027-1034
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1 The effect of several metabotropic ligands and di- or tripeptides were tested on the binding of [3H]-L(+)-2-amino-4-phosphonobutyric acid ([3H]-L-AP4) on rat mGlu4 receptor. For selected compds., the functional activity was determined on this receptor using the guanosine-5'[γ-35S]-thiotriphosphate [γ-35S]-GTP binding assay. 2 Using the scintillation proximity assay, [3H]-L-AP4 saturation anal. gave binding parameters KD and Bmax values of 150 nM and 9.3 pmoles mg-1 protein, resp. The specific binding was inhibited concentration-dependently by several mGlu receptor ligands, and their rank order of affinity was established. 3 Several peptides inhibited the [3H]-L-AP4 binding with the following rank order of potency: glutamate-glutamate > glutamate-glutamate-leucine = aspartate-glutamate > > glutamate-glutamate-aspartate > lactoyl-glutamate > > aspartate-aspartate. Aspartate-phenylalanine-Me ester (aspartame) was inactive up to 1 mM and guanosine-5'-monophosphate and inosine-5'-monophosphate were inactive up to 100 μM. 4 The [γ-35S]-GTP binding functional assay was used to determine the agonist activities of the different compds. For the rat mGlu4 agonists, L-AP4 and L-glutamate, the correlation between their occupancy and activation of the receptor was close to one. The peptides, Glu-Glu, Asp-Glu and Glu-Glu-Asp failed to stimulate the [γ-35S]-GTP binding at receptor occupancy greater than 80% and Glu-Glu-Leu appeared to be a weak partial agonist. These peptides did not elicit a clear dose-dependent umami perception. However, Glu-lac showed a good correlation between its potency to stimulate the [γ-35S]-GTP binding and its affinity for displacement of [3H]-L-AP4 binding. These data are in agreement with the peptide taste assessment in human subjects, which showed that the acid derivs. of glutamate had characteristics similar to umami.
IT 157381-42-5
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition effect on L(+)-2-amino-4-phosphonobutyric acid binding on rat mGlu4a receptor)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

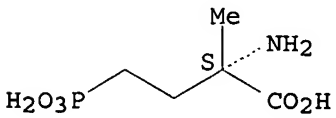


REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 16 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:265035 HCAPLUS
DOCUMENT NUMBER: 131:39859
TITLE: Ligand binding to the amino-terminal domain of the mGluR4 subtype of metabotropic glutamate receptor
AUTHOR(S): Han, Guangming; Hampson, David R.
CORPORATE SOURCE: Faculty of Pharmacy and Department of Pharmacology, University of Toronto, Toronto, ON, M5S 252, Can.
SOURCE: Journal of Biological Chemistry (1999), 274(15), 10008-10013
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The metabotropic glutamate receptor (mGluR) 4 subtype of metabotropic glutamate receptor is a presynaptic receptor that modulates neurotransmitter release. We have characterized the properties of a truncated, epitope-tagged construct containing part of the extra-cellular amino-terminal domain of mGluR4. The truncated receptor was secreted into the cell culture medium of transfected human embryonic kidney cells. The oligomeric structure of the soluble truncated receptor was assessed by gel electrophoresis. In the presence of high concns. of a reducing agent, the truncated receptor migrated as a monomer; at lower concns. of the reducing agent, only higher mol. weight oligomers were observed Competition binding expts. using the radiolabeled agonist [3H]L-2-amino-4-phosphonobutyric acid revealed that the rank order of potency of metabotropic ligands at the truncated receptor was similar to that of the full-length membrane-bound receptor. However, the truncated receptor displayed higher affinities for agonists and lower affinities for antagonists compared with the full-length receptor. Deglycosylation produced a shift in the relative mol. weight of the soluble protein from Mr = 71,000 to Mr = 63,000; deglycosylation had no effect on the binding of [3H]L-2-amino-4-phosphonobutyric acid, indicating that the asparagine-linked carbohydrates are not necessary for agonist binding. These results demonstrate that although the primary determinants of ligand binding to mGluR4 are contained within the first 548 amino acids of the receptor, addnl. amino acids located downstream of this region may influence the affinity of ligands for the binding site.
IT 157381-42-5
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ligand binding to amino-terminal domain of mGluR4 subtype of metabotropic glutamate receptor)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 17 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:238201 HCAPLUS
DOCUMENT NUMBER: 131:167854

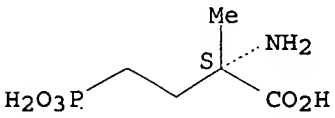
TITLE: Origin of neuronal-like receptors in Metazoa: cloning of a metabotropic glutamate/GABA-like receptor from the marine sponge Geodia cydonium
AUTHOR(S): Perovic, Sanja; Krasko, Anatoli; Prokic, I.; Muller, Isabel M.; Muller, W. E. G.
CORPORATE SOURCE: Abteilung Angewandte Molekularbiologie, Institut fur Physiologische Chemie, Universitat Mainz, Mainz, D-55099, Germany
SOURCE: Cell & Tissue Research (1999), 296(2), 395-404
CODEN: CTSRCS; ISSN: 0302-766X
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Isolated cells from the marine sponge G. cydonium are shown to react to the excitatory amino acid glutamate with an increase in the concentration of intracellular calcium ([Ca2+]i). This effect can also be observed when the compds. L-quisqualic acid (L-QA) or L-(+)-2-amino-4-phosphonobutyric acid (L-AP-4) are used. The effect of L-QA and L-AP-4, both agonists for metabotropic glutamate receptors (mGluRs), can be abolished by the antagonist of group I mGluRs, (RS)-α-methyl-4-carboxyphenylglycine. These data suggest that sponge cells contain an mGluR-like protein. A cDNA encoding rat mGluR subtype 1 has been used to identify the complete nucleotide sequence of G. cydonium cDNA coding for a 528-amino-acid-long protein (59 kDa) that displays marked overall similarity to mGluRs and to GABAergic B receptors. The deduced sponge polypeptide, termed putative mGlu/GABA-like receptor, displays the highest similarity to the 2 families of metabotropic receptors within the transmembrane segment. The N-terminal part of the sponge sequence shows similarity to mGluR4 and mGluR5. These findings suggest that the earliest evolutionary metazoan phylum, the Porifera, possesses a sophisticated intercellular communication and signaling system, as seen in the neuronal network of higher Metazoa.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cloning of a metabotropic glutamate/GABA-like receptor from marine sponge)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 18 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:139854 HCAPLUS
DOCUMENT NUMBER: 130:153794
TITLE: Method for producing glufosinate and intermediate products for the same
INVENTOR(S): Willms, Lothar
PATENT ASSIGNEE(S): Hoechst Schering Agrevo G.m.b.H., Germany
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909039	A1	19990225	WO 1998-EP5053	19980808 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19736125	A1	19990225	DE 1997-19736125	19970820 <--
CA 2301181	A1	19990225	CA 1998-2301181	19980808 <--
AU 9892598	A	19990308	AU 1998-92598	19980808 <--
AU 756471	B2	20030116		
EP 1005475	A1	20000607	EP 1998-945195	19980808 <--
EP 1005475	B1	20040121		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT, IE, FI				
TR 200000456	T2	20000721	TR 2000-200000456	19980808 <--
BR 9811971	A	20000815	BR 1998-11971	19980808 <--
HU 200003501	A2	20010328	HU 2000-3501	19980808 <--
JP 2001515084	T	20010918	JP 2000-509718	19980808 <--
AT 258180	T	20040215	AT 1998-945195	19980808
PT 1005475	T	20040630	PT 1998-945195	19980808
ES 2214727	T3	20040916	ES 1998-945195	19980808
RU 2275376	C2	20060427	RU 2000-107139	19980808
PL 191587	B1	20060630	PL 1998-338855	19980808
IN 1998MA01817	A	20050304	IN 1998-MA1817	19980812
TW 530063	B	20030501	TW 1998-87113567	19980818
ZA 9807465	A	19990222	ZA 1998-7465	19980819 <--
US 6359162	B1	20020319	US 2000-486031	20000217 <--
PRIORITY APPLN. INFO.:			DE 1997-19736125 A	19970820
			WO 1998-EP5053 W	19980808

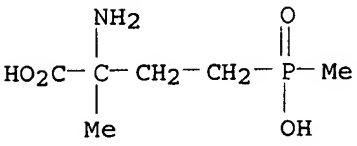
OTHER SOURCE(S): CASREACT 130:153794; MARPAT 130:153794

AB According to the invention, glufosinate (herbicide; (D,L)-2-amino-4-[hydroxy-(methyl)phosphinyl]butanoic acid, MeP(O)(OH)CH2CH2CH(NH2)(CO2H)) and their 2-Me analogs are produced in a multi-stage synthesis from Me phosphorus compds. MePR1R2 (R1, R2 = halo, C1-18 alkoxy, PhCH2O, PhO, OH, etc.) with unsatd. keto compds. CH2:CHC(O)R (R = H, C1-4 alkyl, etc.) via adducts, subsequent reaction in Strecker synthesis conditions and finally, hydrolysis of the aminonitrile. Various compds. are identifiable as adducts, depending on the method conditions and substrates. Thus, reaction of Me vinyl ketone with MeP(OEt)2 in the presence of Ac2O followed by treatment with NaCN in NH3 solution and acidic hydrolysis of aminonitrile gave 94.5% 2-amino-2-methyl-4-(hydroxymethylphosphinyl)butanoic acid ammonium salt.

IT 220288-10-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of herbicide glufosinate derivs. and intermediate products)

RN 220288-10-8 HCAPLUS

CN Isovaline, 4-(hydroxymethylphosphinyl)-, ammonium salt (9CI) (CA INDEX NAME)



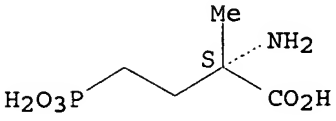
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 19 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:25334 HCAPLUS
DOCUMENT NUMBER: 130:177836
TITLE: Roles of metabotropic glutamate receptor subtypes in modulation of pentylenetetrazole-induced seizure activity in mice
AUTHOR(S): Thomsen, Christian; Dalby, Nils Ole
CORPORATE SOURCE: Novo Nordisk A/S, Health Care Discovery, Malov, DK-2760, Den.
SOURCE: Neuropharmacology (1998), 37(12), 1465-1473
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The anticonvulsant or proconvulsant properties of ligands at metabotropic glutamate receptors (mGluRs) were examined in a chemoconvulsant model using pentylenetetrazole (PTZ). Mice received mGluR ligands by intracerebroventricular (i.c.v.) infusion prior to a s.c. injection of PTZ and the latency to onset of tonic convulsions was recorded. The group I mGluR antagonist 1-aminoindan-1,5-dicarboxylic acid (AIDA) dose-dependently antagonized PTZ-induced seizures with a mean ED50 value of 465 nmol. In contrast, the selective group I mGluR agonist, (S)-3,5-dihydroxyphenylglycine [(S)-DHPG], was proconvulsive and decreased the PTZ-induced seizure latency (ED50 = 60 nmol i.c.v.). A selective agonist of group II mGluRs, (1S,3S)-1-aminocyclopentane dicarboxylic acid [(1S,3S)-ACPD], was proconvulsive but did not affect PTZ-induced seizure latency. Moreover, the proconvulsant effect of (1S,3S)-ACPD was not blocked by the mGluR2 antagonist, α-methylserine-O-phosphate monophenyl ester but was blocked by AIDA suggesting the involvement of group I mGluRs. (2S,1'S,2'S,3'R)-2-(2'-carboxy-3'-phenylcyclopropyl)glycine (PCCG-IV), which is a potent mGluR2 antagonist and a group III mGluR agonist at higher doses, increased the PTZ-induced seizure latency (ED50 = 51 nmol) and this effect was fully reversed by the group III mGluR antagonist, (S)-2-amino-2-methyl-4-phosphonobutanoic acid (MAP4). Similarly, the group III mGluR agonist 1-amino-3-(phosphonomethylene)cyclobutanecarboxylate (cyclobutylene-AP5) increased the PTZ-induced seizure latency (ED50 = 12 nmol) in a MAP4-sensitive manner. Collectively, these data suggest that mGluR ligands modulate PTZ-induced seizure activity in mice by either antagonizing group I mGluRs or activating group III mGluRs.

IT 157381-42-5
RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(metabotropic glutamate receptor subtypes in modulation of pentylenetetrazole-induced seizure activity in mice)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



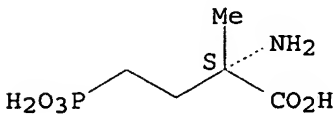
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 20 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:425078 HCAPLUS
DOCUMENT NUMBER: 129:157039
TITLE: A [35S]GTPγS binding assessment of metabotropic glutamate receptor standards in Chinese hamster ovary cell lines expressing the human metabotropic receptor subtypes 2 and 4
AUTHOR(S): Kowal, Dianne; Hsiao, Chu-Lai; Ge, Albert; Wardwell-Swanson, Judith; Ghosh, Krishnendu; Tasse, Rene
CORPORATE SOURCE: CNS Disorders, Wyeth-Ayerst Research, Princeton, NJ, 08543, USA
SOURCE: Neuropharmacology (1998), 37(2), 179-187
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The activities of metabotropic glutamate receptor (mGluR) stds. were evaluated in the [35S]GTPγS binding assay and in the forskolin (FSK)-enhanced cAMP assay using Chinese hamster ovary (CHO) cells or homogenates which expressed the human mGluR (hmGluR) subtypes 2 and 4. Though distinct rank orders of activities were determined for the agonists between the cell lines expressing individual hmGluRs, similar rank orders of agonist activities were determined for the stds. between assays. O-phospho-L-serine (L-SOP) and (S)-2-amino-2-methyl-4-phosphonobutanoic acid (MAP4) antagonized agonist EC90 responses in the cell lines expressing the hmGluR 2 and 4 subtypes, resp. In addition to its antagonist effect, L-SOP increased the baseline level of cAMP when tested in the absence of agonist. In spite of this anomalous effect, L-SOP was found to be a competitive antagonist in the cAMP assay as well as in the [35S]GTPγS binding assay with a pA2 value of 5.2 in both assays. MAP4 was a competitive antagonist of L(+)-2-amino-4-phosphonobutyric acid (L-AP4)-induced responses in the CHO cell line expressing hmGluR4 with pA2 values of 4.4 and 4.5 determined in the [35S]GTPγS binding and cAMP assays, resp. This investigation provides support for the use of the [35S]GTPγS binding assay for in vitro evaluation of substances that interact with mGluRs.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
([35S]GTPγS binding assessment of metabotropic glutamate receptor stds. in Chinese hamster ovary cell lines expressing human metabotropic receptor subtypes 2 and 4)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

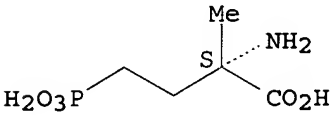
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 21 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:234229 HCAPLUS
DOCUMENT NUMBER: 128:317182
TITLE: (+)-MCPG blocks induction of LTP in CA1 of rat hippocampus via agonist action at an mGluR group II receptor
AUTHOR(S): Breakwell, N. A.; Rowan, M. J.; Anwyl, R.
CORPORATE SOURCE: Department of Physiology Trinity College, University of Dublin, Dublin, 2, Ire.
SOURCE: Journal of Neurophysiology (1998), 79(3), 1270-1276
CODEN: JONEA4; ISSN: 0022-3077
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated the effect of metabotropic glutamate receptor (mGluR) ligands on the induction of long-term potentiation (LTP) of field excitatory postsynaptic potentials (EPSPs) in CA1 of rat hippocampus, in particular the manner by which the nonsubtype selective mGluR ligand α-methyl-4-carboxyphenylglycine [(+)-MCPG] blocks LTP induction. Normalized control LTP was blocked by (+)-MCPG (250 μM), but not by the mGluRI selective antagonist (S)-4-carboxyphenylglycine (4-CPG), the mGluRII selective antagonist 1/(2S,3S,4S)-2-methyl-2-(carboxy-cyclopropyl)glycine (MCCG), or the mGluRIII antagonist (S)-2-amino-2-methyl-4-phosphonobutanoic acid/α-Me (MAP4). In contrast the mGluRII agonist {(1S,3S)-1-aminocyclopentane-1,3-dicarboxylic acid [(1S,3S)-ACPD]; 10 or 25 μM} completely and consistently blocked LTP. The block of LTP by both (1S,3S)-ACPD and (+)-MCPG could be prevented by preincubation with the mGluRII antagonist MCCG. These studies demonstrate that (+)-MCPG blocks LTP induction through an agonist action at an mGluRII receptor and not through a nonselective antagonist action.
IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
((+)-MCPG blocks induction of LTP in CA1 of rat hippocampus via agonist action at an mGluR group II receptor)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

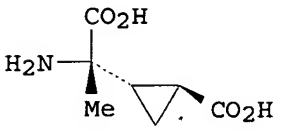
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 22 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:241459 HCAPLUS
DOCUMENT NUMBER: 126:330807
TITLE: Synthesis of (2S,1'S,2'S)-2-methyl-2-(carboxycyclopropyl)glycine and (S)-2-amino-2-methyl-4-phosphonobutyric acid from L-alanine
AUTHOR(S): Ma, Dawei; Ma, Zahaochun; Jian, Jiquing; Yang, Zhen; Zheng, Chongzhi
CORPORATE SOURCE: Shanghai Inst. Org. Chemistry, Chinese Academy

Science, Shanghai, 200032, Peop. Rep. China
SOURCE: Tetrahedron: Asymmetry (1997), 8(6), 889-893
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:330807
GI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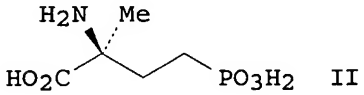
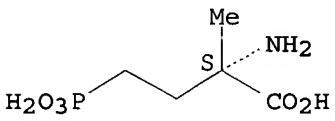

II

AB The synthesis of title compds. I and II, two isotype-selective antagonists for metabotropic glutamate receptors, from L-alanine is described.
IT 157381-42-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of glutamate receptor antagonists (carboxycyclopropyl)glycine and amino(methyl)phosphonobutyric acid from alanine)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

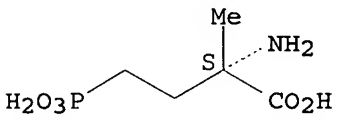
L34 ANSWER 23 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:212439 HCAPLUS
DOCUMENT NUMBER: 126:287949
TITLE: Attenuation of morphine withdrawal symptoms by subtype-selective metabotropic glutamate receptor antagonists
AUTHOR(S): Fundytus, Marian E.; Ritchie, Jennifer; Coderre, Terence J.
CORPORATE SOURCE: Pain Mechanisms Laboratory, Clinical Research Institute of Montreal, Universite de Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: British Journal of Pharmacology (1997), 120(6), 1015-1020
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have previously shown that chronic antagonism of group I metabotropic glutamate receptors (mGluRs), in the brain, attenuates the precipitated morphine withdrawal syndrome in rats. In the present investigation the authors assessed the effects of chronic antagonism of group II and III mGluRs on the severity of withdrawal symptoms in rats treated chronically with s.c. morphine. Concurrently with s.c. morphine the authors infused intracerebroventricularly (i.c.v.) one of a series of phenylglycine derivs. selective for specific mGluR subtypes. Group II mGluRs

(mGluR2,3), which are neg. coupled to adenosine 3':5'-cyclic monophosphate (cAMP) production, were selectively antagonized with 2s, 1's, 2's-2-methyl-2-(2'-carboxycyclopropyl) glycine (MCCG). Group III mGluRs (mGluR4,6,7 and 8), which are also neg. linked to cAMP production, were selectively antagonized with α-methyl-L-amino-4-phosphonobutanoate (MAP4). The effects of MCCG and MAP4 were compared with α-methyl-4-carboxyphenylglycine (MCPG), which non-selectively antagonizes group II mGluRs, as well as group I mGluRs (mGluR1,5) which are pos. coupled to phosphatidylinositol (PI) hydrolysis. Chronic i.c.v. administration of both MCCG and MAP4 significantly decreased the time spent in withdrawal, MCPG and MCCG reduced the frequency of jumps and wet dog shakes and attenuated the severity of agitation. Acute i.c.v. injection of mGluR antagonists just before the precipitation of withdrawal failed to decrease the severity of abstinence symptoms. Rather, acute i.c.v. injection of MCCG significantly increased the time spent in withdrawal. Our results suggest that the development of opioid dependence is affected by mGluR-mediated PI hydrolysis and mGluR-regulated cAMP production

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuation of morphine withdrawal symptoms by subtype-selective metabotropic glutamate receptor antagonists in rats)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 24 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1997:199511 HCAPLUS
DOCUMENT NUMBER:	126:287919
TITLE:	Two phenylglycine derivatives antagonize responses to L-AP4 in ON bipolar cells of the amphibian retina
AUTHOR(S):	Thoreson, W. B.; Gottesman, J.; Jane, D. E.; Tse, Heong-Wai; Watkins, J. C.; Miller, R. F.
CORPORATE SOURCE:	Departments of Ophthalmology and Pharmacology, University of Nebraska Medical Center, Omaha, NE, 68198-5540, USA
SOURCE:	Neuropharmacology (1997), 36(1), 13-20 CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER:	Elsevier
DOCUMENT TYPE:	Journal
LANGUAGE:	English

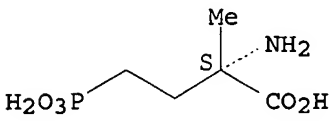
AB Light responses of retinal ON bipolar cells are mediated by metabotropic glutamate receptors selectively activated by L-2-amino-4-phosphonobutyric acid (L-AP4). Antagonists to L-AP4 receptors in ON bipolar cells have not previously been identified. This study examines the electrophysiol. effects of (S)-2-amino-2-methyl-4-phosphonobutanoic acid (MAP4), (RS)-4-chloro-3,5-dihydroxyphenylglycine (CDHPG) and (RS)-3,4,5-trihydroxyphenylglycine (THPG), at L-AP4 receptors in ON bipolar cells of the amphibian retina. Unlike its actions in spinal cord, in retinal ON bipolar cells MAP4 is a weak agonist which exhibits no detectable antagonism to L-AP4. On the other hand, CDHPG exhibits a mixture of agonist and antagonist properties. Addition of Co2+ and oxygenation of CDHPG turns the solution brown and enhances antagonist effects, suggesting that the antagonism reflects actions of a breakdown product of CDHPG. Although

THPG did not prove to be this breakdown product, it also has electrophysiol. effects consistent with an L-AP4 receptor antagonist. The results suggest that THPG and breakdown products of CDHPG may be antagonists to L-AP4 receptors in retinal ON bipolar cells, although the possibility that these compds. antagonize effects of L-AP4 by acting at some site in the transduction pathway of L-AP4 receptors cannot yet be excluded.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(phenylglycine derivs. as L-AP4 receptor antagonists in retina)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



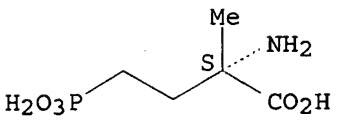
L34 ANSWER 25 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:171653 HCAPLUS
DOCUMENT NUMBER: 126:233539
TITLE: Convulsant and anticonvulsant actions of agonists and antagonists of group III mGluRs
AUTHOR(S): Ghauri, Mamoona; Chapman, Astrid G.; Meldrum, Brian S.
CORPORATE SOURCE: Department of Neurology, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF, UK
SOURCE: NeuroReport (1996), 7(9), 1469-1474
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Rapid Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB GROUP III metabotropic glutamate receptors (mGluR4, 6, 7, 8) are neg. coupled to adenylate cyclase and, when activated presynaptically, decrease the release of glutamate and GABA. We have used intracerebroventricular injections of agonists and antagonists believed to act selectively on these receptors to study the pro- or anti-convulsant effects of mGluR III activation in non-epileptic (Swiss-Webster) and epileptic (DBA/2) mice. In both mouse strains the prototypic agonists L-2-amino-4-phosphonobutanoate (LAP4) and L-serine-O-phosphate are proconvulsant. The supposed antagonists (S)-2-methyl-2-amino-4-phosphonobutanoate (MAP4) and (RS)-α-methyl-4-phosphonophenylglycine (MPPG), have a predominantly proconvulsant effect. (S)-α-methyl-3-carboxyphenylalanine, which is a potent and selective antagonist for LAP4 in the cortex, is anticonvulsant in DBA/2 mice and decreases the convulsant effect of N-methyl-D-aspartate, 3,5-dihydroxyphenylglycine, LAP4 and MPPG in Swiss-Webster mice. These data suggest that reduced inhibitory transmission may be more significant than reduced synaptic release of glutamate following group III mGluR activation.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(convulsant and anticonvulsant actions of agonists and antagonists of group III metabotropic glutamate receptors)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

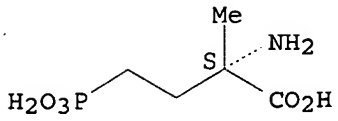


L34 ANSWER 26 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:86875 HCAPLUS
DOCUMENT NUMBER: 126:181683
TITLE: Epileptogenesis in vivo enhances the sensitivity of inhibitory presynaptic metabotropic glutamate receptors in basolateral amygdala neurons in vitro
AUTHOR(S): Neugebauer, Volker; Keele, N. Bradley; Shinnick-Gallagher, Patricia
CORPORATE SOURCE: Department of Pharmacology and Toxicology, The University of Texas Medical Branch, Galveston, TX, 77555-1031, USA
SOURCE: Journal of Neuroscience (1997), 17(3), 983-995
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Modulation of excitatory synaptic transmission by presynaptic metabotropic glutamate receptors (mGluRs) was examined in brain slices from control rats and rats with amygdala-kindled seizures. Using whole-cell voltage-clamp and current-clamp recordings, this study shows for the first time that in control and kindled basolateral amygdala neurons, two pharmacol. distinct presynaptic mGluRs mediate depression of synaptic transmission. Moreover, in kindled neurons, agonists at either group II- or group III-like mGluRs exhibit a 28- to 30-fold increase in potency and suppress synaptically evoked bursting. The group II mGluR agonist (2S,3S,4S)-2-(carboxycyclopropyl)glycine (L-CCG) dose-dependently depressed monosynaptic EPSCs evoked by stimulation in the lateral amygdala with EC50 values of 36 nM (control) and 1.2 nM (kindled neurons). The group III mGluR agonist L-2-amino-4-phosphonobutyrate (L-AP4) was less potent, with EC50 values of 297 nM (control) and 10.8 nM (kindled neurons). The effects of L-CCG and L-AP4 were fully reversible. Neither L-CCG (0.0001-10 μM) nor L-AP4 (0.001-50 μM) caused membrane currents or changes in the current-voltage relationship. The novel mGluR antagonists (2S,3S,4S)-2-methyl-2-(carboxycyclopropyl)-glycine (MCCG; 100 μM) and (S)-2-methyl-2-amino-4-phosphonobutyrate (MAP4; 100 μM) selectively reversed the inhibition by L-CCG and L-AP4 to 81.3% and 65.3% of predrug, resp. MCCG and MAP4 (100-300 μM) themselves did not significantly affect synaptic transmission. The exquisite sensitivity of agonists in the kindling model of epilepsy and the lack of evidence for endogenous receptor activation suggest that presynaptic group II- and group III-like mGluRs might be useful targets for suppression of excessive synaptic activation in neurol. disorders such as epilepsy.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(epileptogenesis enhances inhibitory presynaptic metabotropic glutamate receptor sensitivity in basolateral amygdala neurons)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



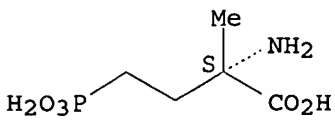
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 27 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:762379 HCAPLUS
DOCUMENT NUMBER: 126:45516
TITLE: L-AP4 (L-(+)-2-amino-4-phosphonobutyric acid) induced impairment of spatial learning in the rat is antagonized by MAP4 ((S)-2-amino-2-methyl-4-phosphonobutanoic acid)
AUTHOR(S): Hoelscher, Christian; McGlinchey, Liam; Rowan, Michael J.
CORPORATE SOURCE: Dep. Pharmacology, Trinity College, Dublin, Ire.
SOURCE: Behavioural Brain Research (1996), 81(1/2), 69-79
CODEN: BBREDI; ISSN: 0166-4328
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB L-AP4, an agonist at the metabotropic glutamate receptors 4, 6, 7, 8 and 9 produced a selective spatial learning impairment in a water maze as well as in an 8-arm maze task when injected i.c.v. (5 μl of a 80 mM solution), a dose previously reported to block consolidation of long-term potentiation in vivo. Acquisition and recall of the spatial water-maze task, as measured by escape latency and quadrant bias, resp., were impaired, whereas swim speed was not affected. In contrast, ability to perform a non-spatial control task was not impaired; latency to reach a visible escape platform was not delayed in L-AP4-treated animals. No behavioral difference was visible in the open field. MAP4, an antagonist of mGluRs mediating L-AP4 induced reduction of transmitter release, when administered pretraining i.c.v. (5 μl of an 80 mM solution) did not affect motor activity in the open field test but did impair learning of both spatial tasks. In addition, swim speed was increased. However, injecting L-AP4 and MAP4 in combination at equimolar concns. had no effect on learning in both spatial tasks or on swim speed in the water maze. Neither latency in the visible-platform test nor behavior in the open field was affected. We conclude that L-AP4 sensitive metabotropic glutamate receptors play a selective role in learning and memory formation of the rat.

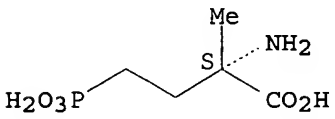
IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(L-AP4 (L-(+)-2-amino-4-phosphonobutyric acid) induced impairment of spatial learning in the rat is antagonized by MAP4 ((S)-2-amino-2-methyl-4-phosphonobutanoic acid))
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 28 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:680367 HCAPLUS
DOCUMENT NUMBER: 126:31629
TITLE: Phosphono substituted amino acids as selective metabotropic glutamate receptor antagonists
AUTHOR(S): Jane, David E.; Pittaway, Kay; Sunter, David C.; Thomas, Nicola K.; Tse, Heong-Wai
CORPORATE SOURCE: Dep. Pharmacol., Sch. Med. Scis., Bristol, BS8 1TD, UK
SOURCE: Phosphorus, Sulfur and Silicon and the Related Elements (1996), 109-110(1-4, Proceedings of the Thirteenth International Conference on Phosphorus Chemistry, 1995), 313-316
CODEN: PSSLEC; ISSN: 1042-6507
PUBLISHER: Gordon & Breach
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A conference report. New phosphono substituted amino acid antagonists have been prepared and used to discriminate between different types of presynaptic metabotropic glutamate receptors (mGluRs) in the neonatal rat spinal cord that are activated selectively by L-2-amino-4-phosphonobutanoate (L-AP4) and (1S,3S)-1-aminocyclopentane-1,3-dicarboxylate [(1S,3S)-ACPD]. (RS)-α-Methyl-4-phosphonophenylglycine (MPPG; KD 9.2.μM), (S)-2-amino-2-methyl-4-phosphonobutanoate (MAP4; KD 22 MM) and (RS)-α-methylserine-O-phosphate (MSOP; KD 51 μM) were potent and selective antagonists of L-AP4-activated mGluRs. (RS)-α-Methyl-4-tetrazolylphenylglycine (MTPG; KD 77 μM) and (RS)-α-methylserine-O-phosphate monophenylphospho ester (MSOPPE; KD 73 μM) were moderately potent and preferential antagonists of (1S,3S)-ACPD-activated mGluRs. Structure-activity relationships are briefly discussed.
IT 157381-42-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(phosphono substituted amino acids as selective metabotropic glutamate receptor antagonists)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 29 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:655388 HCAPLUS
DOCUMENT NUMBER: 126:1515
TITLE: Coupling of metabotropic glutamate receptors 2 and 4 to Gα15, Gα16, and chimeric Gαq/i proteins: characterization of new antagonists
AUTHOR(S): Gomeza, Jesus; Mary, Sophie; Brabet, Isabelle; Parmentier, Marie-Laure; Restituito, Sophie; Bockaert, Joel; Pin, Jean-Philippe
CORPORATE SOURCE: UPR Centre Nationale de Recherche Scientifique 9023, Mecanismes Moleculaires des Communications Cellulaires, Montpellier, 34094, Fr.
SOURCE: Molecular Pharmacology (1996), 50(4), 923-930

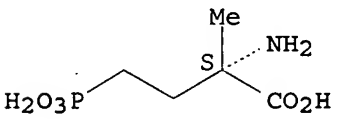
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Together with the calcium-sensing receptor, the metabotropic glutamate receptors (mGluRs) share no sequence homol. with the other G protein-coupled receptors (GPCRs) and therefore constitute a new family of receptors. Recently, it was reported that Gα15 and Gα16 subunits allow many GPCRs to activate phospholipase C (PLC). Furthermore, the exchange of a few C-terminal residues of Gαq by those of Gαi2 or Gαo allows the resulting chimeric Gα subunits (Gαqi and Gαqo, resp.) to couple Gi-coupled receptors to PLC. The authors report that mGluR2 and mGluR4, two receptors neg. coupled to adenylyl cyclase, activate PLC when coexpressed with Gα15, Gαqi, or Gαqo. This indicates that the C-terminal end of the Gα subunit also plays an important role in the specific interaction between mGluRs and the G proteins. In addition, the measurement of PLC activation by Gi-coupled mGluRs coexpressed with these Gα subunits constitutes an easy functional assay for the pharmacol. characterization of these receptors. The rank order of potency of antagonists was (2S,3S,4S)-2-methyl-2-(carboxycyclopropyl)glycine ≈ (R,S)-α-methyl-4-phosphonophenylglycine > (R,S)-α-methyl-4-sulfonophenylglycine > (R,S)-α-methyl-4-tetrazolylphenylglycine = (S)-2-amino-2-methyl-4-phosphonobutyrate for mGluR2 and (R,S)-α-methyl-4-phosphonophenylglycine ≥ (S)-2-amino-2-methyl-4-phosphonobutyrate » (R,S)-α-methyl-4-sulfonophenylglycine [(R,S)-α-methyl-4-tetrazolylphenylglycine and (2S,3S,4S)-2-methyl-2-(carboxycyclopropyl)glycine being inactive at 1 mM] for mGluR4. Using this functional assay, (R,S)-α-methyl-4-phosphonophenylglycine was found to have a similar KB value for mGluR2 and mGluR4.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(coupling of metabotropic glutamate receptors 2 and 4 to Gα15, Gα16, and chimeric Gαq/i proteins and characterization of new antagonists)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

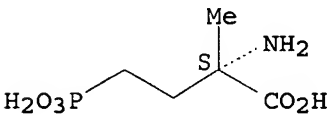
Absolute stereochemistry. Rotation (+).



L34 ANSWER 30 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:544848 HCAPLUS
DOCUMENT NUMBER: 125:266366
TITLE: Characterization of the metabotropic glutamate receptors (mGluRs) which modulate GABA-mediated inhibition in the ventrobasal thalamus
AUTHOR(S): Salt, T. E.; Eaton, S. A.; Turner, J. P.
CORPORATE SOURCE: Institute Ophthalmology, University College London, London, EC1V 9EL, UK
SOURCE: Neurochemistry International (1996), 29(3), 317-322
CODEN: NEUIDS; ISSN: 0197-0186
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ventrobasal thalamus (VB) relays and processes somatosensory information ascending to the cerebral cortex. Several types of mGluR are known to be present in VB, and we have previously shown that Group II and Group III mGluR agonists can reduce inhibitory synaptic transmission by acting at presynaptic receptors on GABAergic terminals in this structure. We have tested the action of several antagonists against the disinhibitory action of the Group II agonist CCG-I [(2S,3S,4S)-α-(carboxy-cyclopropyl)-glycine] and the Group III agonist L-AP4 [L-2-amino-4-phosphonobutyrate] in the VB of anesthetized rats using extracellular single-neuron recording techniques and iontophoretic applications of mGluR antagonists and agonists. The antagonists MAP4 [α-methyl-L-AP4] and MPPG [(±)-α-methyl-4-phosphonophenylglycine] reduced the disinhibitory actions of L-AP4 while having little effect on the disinhibitory action of CCG-I. In contrast, MCCG [α-methyl-CCG-I] and MCPG [(+)-α-methyl-4-carboxyphenylglycine] antagonized CCG-I, while having less effect against L-AP4 responses. These results support the hypothesis that GABAergic inhibitory transmission in VB can be modulated by at least two types of mGluR, belonging to Group II and Group III. Furthermore, the novel antagonists appear to be useful tools for the future study of the physiol. role of these receptors in thalamic sensory processing.
IT 157381-42-5, α-Methyl-L-AP 4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(metabotropic glutamate receptors modulation of GABA-mediated inhibition in ventrobasal thalamus)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



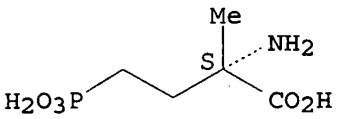
L34 ANSWER 31 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:459362 HCAPLUS
DOCUMENT NUMBER: 125:212381
TITLE: Agonists of cyclic AMP-coupled metabotropic glutamate receptors in adult rat cortical slices
AUTHOR(S): Kemp, Martyn C.; Jane, David E.; Tse, Heong-Wai; Roberts, Peter J.
CORPORATE SOURCE: Department of Pharmacology, School of Medical Sciences, University of Bristol, Bristol, UK
SOURCE: European Journal of Pharmacology (1996), 309(1), 79-85
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A number of potential Group 2 and Group 3 metabotropic glutamate receptor (mGlu receptor) agonists were investigated in adult rat brain cerebrocortical slices. The rank order of their potency in inhibiting forskolin-stimulated adenylyl cyclase was : (S)-2-amino-2-methyl-4-phosphonobutyric acid (MAP4)>(2S,1' S,2'S)-2-(2-carboxycyclopropyl)glycine (L-CCG-I)>(1S,3 S)-1-aminocyclopentane-1,3-dicarboxylic acid (1S,3S-ACPD)> (1S,3R)-1-aminocyclopentane-1,3-dicarboxylic acid (1S,3R

-ACPD)>(2S,1'R,2'R,3'R)-2-(2,3-dicarboxycyclopropyl)glycine (DCG-IV)>(S)-2-methylglutamate ((S)-MG)>L-glutamate> (2S,1'S,2'S)-2-(2-carboxycyclopropyl)alanine (MCCG)>L -2-amino-4-phosphonobutyric acid (L-AP4)>L-serine-O-phosphate (SOP). The finding that (S)-2-amino-2-methyl-4-phosphonobutyric acid was the most potent agonist at these metabotropic glutamate receptors is in contrast to its observed potent mGlu receptor antagonist action in the neonatal rat spinal cord.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(agonists of cAMP-coupled metabotropic glutamate receptors in adult rat cortical slices)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 32 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1996:253454 HCAPLUS
DOCUMENT NUMBER:	124:331704
TITLE:	Structure-activity relationships of new agonists and antagonists of different metabotropic glutamate receptor subtypes
AUTHOR(S):	Sekiyama, N.; Hayashi, Y.; Nakanishi, S.; Jane, D. E.; Tse, H. W.; Birse, E. F.; Watkins, J. C.
CORPORATE SOURCE:	Inst. Immunol., Kyoto Univ. Fac. Med., Kyoto, 606, Japan
SOURCE:	British Journal of Pharmacology (1996), 117(7), 1493-503 CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER:	Stockton
DOCUMENT TYPE:	Journal
LANGUAGE:	English

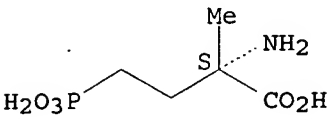
AB The authors investigated the agonist and antagonist activities of 22 new phenylglycine and phenylalanine derivs. for metabotropic glutamate receptors (mGluRs) by examining their effects on the signal transduction of mGluR1, mGluR2 and mGluR6 subtypes expressed in Chinese hamster ovary cells. This anal. revealed several structural characteristics that govern receptor subtype specificity of the agonist and antagonist activities of phenylglycine derivs. Hydroxyphenylglycine derivs. possessed either an agonist activity on MGluR1/mGluR6 or an antagonist activity of mGluR1. Carboxyphenylglycine derivs. showed an agonist activity on mGluR1. α-Methylation or α-ethylation of the carboxyphenylglycine derivs. converts the agonist property from mGluR2 to an antagonist property, thus producing antagonists at both mGluR1 and mGluR2. Structurally-corresponding phenylalanine derivs. showed little or no agonist or antagonist activity on any subtypes of the receptors. The nature and positions of side chains and ring substituents incorporated into the phenylglycine structure are critical in determining the agonist and antagonist activities of members of this group of compds. on different subtypes of the mGluR family. The authors also tested 2 α-Me derivs. of mGluR agonists. (2S, 1'S, 2'S)-2-(2-Carboxycyclopropyl)glycine (L-CCG-I) is a potent agonist for mGluR2 but α-methylation of this compound changes its activity to that of an mGluR2-selective antagonist. In contrast, α-methylation of L-2-amino-4-phosphonobutyrate (L-AP4) results in retention of an agonist activity on mGluR6. Thus,

α-methylation produces different effects, depending on the chemical structures of lead compds. and/or on the subtype of mGluR tested.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structure-activity relations of agonists and antagonists of glutamate receptors)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 33 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:253448 HCAPLUS
DOCUMENT NUMBER: 124:332784
TITLE: Pharmacological antagonism of the actions of group II and II mGluR agonists in the lateral perforant path of rat hippocampal slices
AUTHOR(S): Bushell, Trevor J.; Jane, David E.; Tse, Heong-Wai; Watkins, Jeffrey C.; Garthwaite, John; Collingridge, Graham L.
CORPORATE SOURCE: Dep. Anatomy, Univ. Bristol, Bristol, BS8 1TD, UK
SOURCE: British Journal of Pharmacology (1996), 117(7), 1457-62
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

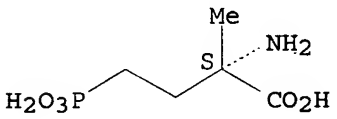
AB An understanding of the physiol. and pathol. roles of metabotropic glutamate receptors (mGluRs) is currently hampered by the lack of selective antagonists. Standard extracellular recording techniques were used to investigate the activity of recently reported mGluR antagonists on agonist-induced depressions of synaptic transmission in the lateral perforant path of hippocampal slices obtained from 12-16 day-old rats. The group III specific mGluR agonist, (S)-2-amino-4-phosphonobutanolate (L-AP4) depressed basal synaptic transmission in a reversible and dose-dependent manner. The mean (±s.e. mean) depression obtained with 100 μM L-AP4 (the maximum concentration tested) was 74±3% and the IC50 value was 3±1 μM (n=5). The selective group II mGluR agonists, (1S,3S)-1-aminocyclopentane-1,3-dicarboxylate [(1S,3S)-ACPD] and (2S,1'R,2'R,3'R)-2-(2',3'-dicarboxycyclopropyl)glycine (DCG-IV) also depressed basal synaptic transmission in a reversible and dose-dependent manner. The mean depression obtained with 200 μM (1S,3S)-ACPD was 83±8% and the IC50 value was 12±3 μM (n=5). The mean depression obtained with 1 μM DCG-IV was 73±7% and the IC50 value was 88±15 nM (n=4). Synaptic depressions induced by the actions of 20 μM (1S,3S)-ACPD and 10 μM L-AP4 were antagonized by the mGluR antagonists, (+)-α-methyl-4-carboxyphenylglycine [(+)-MCPG], (S)-2-methyl-2-amino-4-phosphonobutanoate (MAP4), (2S,1'S,2'S)-2-methyl-(2'-carboxycyclopropyl)glycine (MCCG), (RS)-α-methyl-4-tetrazolylphenylglycine (MTPG), (RS)-α-methyl-4-sulfonophenylglycine (MSPG) and (RS)-α-methyl-4-phosphonophenylglycine (MPPG) (all tested at 500 μM). (+)-MCPG was a weak antagonist of both L-AP4 and (1S,3S)-ACPD-induced depressions. MCCG was selective towards (1S,3S)-ACPD, but anal. of its effects were complicated by apparent partial agonist activity. MAP4 showed good selectivity for L-AP4-induced

effects. The most effective antagonist tested against 10 μM L-AP4 MPPG (mean reversal 90±3%; n=4). In contrast, the most effect antagonist tested against 20 μM (1S,3S)-ACPD induced depressions was MTPG (mean reversal 64±4%; n=4). Both antagonists produced parallel shifts in agonist dose-response curves. Schild anal. yielded estimated KD values of 11.7 μM and 27.5 μM, resp. Neither antagonist had any effect on basal transmission or on depressions induced by the adenosine receptor agonist, 2-chloroadenosine (500 nM; n=3). We conclude that both group II and group III mGluRs can mediate synaptic depressions induced by mGluR agonists in the lateral performant path. The mGluR antagonists MTPG, MPPG and MAP4 should be useful in determining the roles of group II and III mGluRs in the central nervous system.

IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. antagonism of the actions of group II and II mGluR agonists in the lateral perforant path of rat hippocampal slices)

RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 34 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:957967 HCAPLUS
DOCUMENT NUMBER: 124:30404
TITLE: Preparation of α-tetrasubstituted-α-amino acids as central nervous system agents.
INVENTOR(S): Watkins, Jeffrey Clifton; Jane, David Edward
PATENT ASSIGNEE(S): University of Bristol, UK; Tocris Cookson Ltd.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9515940	A1	19950615	WO 1994-GB2690	19941209 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9512469	A	19950627	AU 1995-12469	19941209 <--
EP 733036	A1	19960925	EP 1995-903410	19941209 <--
R: CH, DE, FR, GB, IT, LI, NL				

PRIORITY APPLN. INFO.: GB 1993-25368 A 19931210
WO 1994-GB2690 W 19941209
OTHER SOURCE(S): CASREACT 124:30404; MARPAT 124:30404

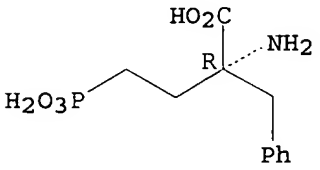
AB R11R12NC(Q)(BY)(R10) [Y = carboxy, phosphono, PO2H(OR13), phosphinco, PO2H(R13), OPO3H2, OPO2(OR13), arsono, AsO2H(OR13), arsenico, AsO2H(R13), sulfo, sulfino, sulpheno, OSO3H, tetrazolyl, 3-hydroxyisoxazolyl, 1,2,4-oxadiazolidin-3,5-dione residue, hydantoin residue; R13 = alkyl,

alkenyl, alkynyl, cycloalkyl, (substituted) aryl, aralkyl; B = (substituted) alkylene, cycloalkylene, alkenylene,alkynylene; Q = carboxy, alkoxycarbonyl, hydroxamic acid residue; R10 = alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, (substituted) aryl, aralkyl, biaryl; R11, R12 = H, alkyl, alkenyl, alkynyl, acyl, (substituted) PhCO; 2 of Y, Q, R10, R11, R12 and the substituents on B being optionally condensed with each other to form a carbocyclic or heterocyclic ring system], were prepared Thus, (2R,5SR)-(-)-2,5-dihydro-3,6-dimethoxy-2-isopropyl-5-methylpyrazine in THF at -78° was treated with BuLi and then Me 4-bromobut-2-enoate in THF to give an oil which was treated successively with CF3CO2H and refluxing aqueous HCl to give 38.7% (2S,1'S,2'S)-2-amino-2-(2'-carboxycycloprop-1'-yl)propanoic acid. Certain title compds. antagonize the ability of L-2-amino-4-phosphonobutyrate to depress forskolin-stimulated cAMP production in rat cerebral cortical tissue; they are said to be more potent and/or selective agonists or antagonists at metabotropic glutamate receptors.

IT 104739-22-2P 157381-42-5P 170984-73-3P
170984-75-5P 171228-34-5P 171483-43-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of α-tetrasubstituted-α-amino acids as central nervous system agents)

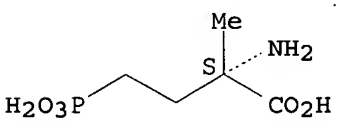
RN 104739-22-2 HCAPLUS
CN D-Phenylalanine, α-(2-phosphonoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



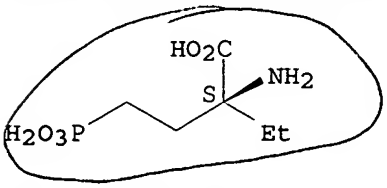
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



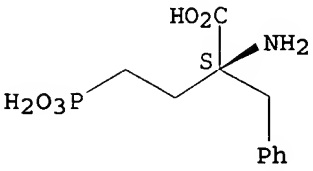
RN 170984-73-3 HCAPLUS
CN Butanoic acid, 2-amino-2-ethyl-4-phosphono-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



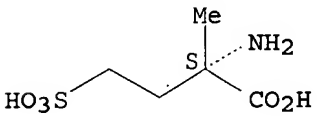
RN 170984-75-5 HCAPLUS
CN L-Phenylalanine, α-(2-phosphonoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



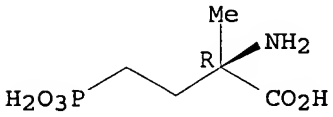
RN 171228-34-5 HCAPLUS
CN L-Isovaline, 4-sulfo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

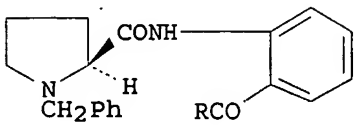


RN 171483-43-5 HCAPLUS
CN D-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 35 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:848204 HCAPLUS
DOCUMENT NUMBER: 124:87695
TITLE: Asymmetric synthesis of hetero-organic analogs of natural compounds. 17. Fluorine-containing esters of S-homocysteic acid
AUTHOR(S): Soloshonok, V. A.; Svistunova, N. Yu.; Kukhar, V. P.; Kuz'mina, N. A.; Popov, V. I.; Belokon, Yu. N.
CORPORATE SOURCE: Institute Bioorganic Chemistry Petrochemistry Academy Sciences Ukraine, Kiev, 253160, Ukraine
SOURCE: Izvestiya Akademii Nauk, Seriya Khimicheskaya (1993), (4), 786-90
CODEN: IASKEA
PUBLISHER: Nauka
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI

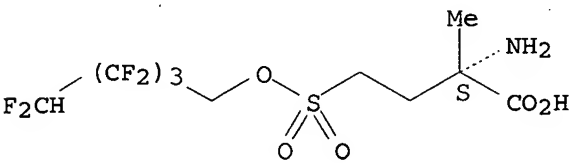


I

AB The Michael addition of CH2:CHSO2OCH2(CF2)4H to Ni(II) complexes of Schiff bases derived from benzylprolines I (R = H, Me) and glycine or alanine is a convenient preparative asym. synthesis of previously unknown fluorinated

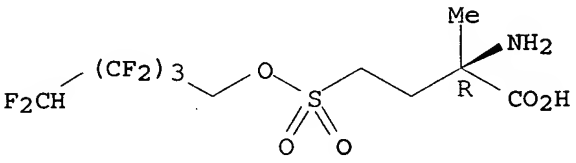
esters of S-homocysteic acid.
IT 172505-76-9P 172505-77-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of fluorine-containing esters of homocysteic acid)
RN 172505-76-9 HCAPLUS
CN L-Isovaline, 4-[[(2,2,3,3,4,4,5,5-octafluoropentyl)oxy]sulfonyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 172505-77-0 HCAPLUS
CN D-Isovaline, 4-[[(2,2,3,3,4,4,5,5-octafluoropentyl)oxy]sulfonyl]- (9CI)
(CA INDEX NAME)

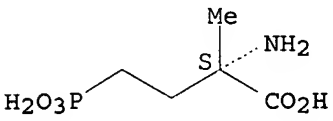
Absolute stereochemistry.



L34 ANSWER 36 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:796443 HCAPLUS
DOCUMENT NUMBER: 123:189159
TITLE: Pharmacological characterization of MCCG and MAP4 at the mGluR1b, mGluR2 and mGluR4a human metabotropic glutamate receptor subtypes
AUTHOR(S): Knoepfel, T.; Lukic, S.; Leonardt, T.; Flor, P. J.; Kuhn, R.; Gasparini, F.
CORPORATE SOURCE: Pharmaceuticals Division, Ciba, Basel, CH 4002, Switz.
SOURCE: Neuropharmacology (1995), 34(8), 1099-102
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 2 reported metabotropic glutamate receptor (mGluR) antagonists, α-methyl-cyclopropyl glycine (MCCG) and α-methyl-aminophosphonobutyrate (MAP4) were tested on the mGluR1b, mGLuR2 and mGluR4a subtypes of human mGluRs. Neither MCCG (500 μM) nor MAP4 (500 μM) antagonized the activation of mGluR1b by 10 μM quisqualate. MCCG was found to potently antagonize the action of 30 μM (1S,3R)-1-aminocyclopentane-1,3-dicarboxylic acid [(1S,3R)-ACPD] at mGluR2 (IC50 = 87.5 μM; apparent KD = 25 μM) but did not block the action of 1 μM S-2-amino-4-phosphonobutyric acid at mGluR4a (IC50 >> 1 mM). MAP4 was a weak antagonist or partial agonist at mGluR4a (IC50 > 500 μM) and, less potently, also antagonized the action of 30 μM (1S,3R)-ACPD at mGluR2 (IC50 .apprx.2 mM).
IT 157381-42-5, α-Methyl-L-AP 4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. characterization of antagonists MCCG and MAP4 at the

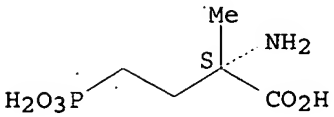
mGluR1b, mGluR2 and mGluR4a human metabotropic glutamate receptor subtypes)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



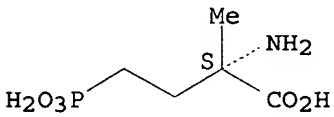
L34 ANSWER 37 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:796430 HCAPLUS
DOCUMENT NUMBER: 123:189152
TITLE: Pharmacological evidence for an involvement of group II and group III mGluRs in the presynaptic regulation of excitatory synaptic responses in the CA1 region of rat hippocampal slices
AUTHOR(S): Vignes, M.; Clarke, V. R. J.; Davies, C. H.; Chambers, A.; Jane, D. E.; Watkins, J. C.; Collingridge, G. L.
CORPORATE SOURCE: Department of Anatomy, The University of Bristol, Bristol, BS8 1TD, UK
SOURCE: Neuropharmacology (1995), 34(8), 973-82
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The actions of 4 mGluR antagonists, (+)-MCPG, MAP4, MCCG and (S)-4CPG, were evaluated against agonist-induced depressions of synaptic transmission at the Schaffer collateral commissural pathway in rat hippocampal slices. (+)-MCPG (1 mM) reversed very effectively depressions of field EPSPs induced by (1S,3R)-ACPD and (1S,3S)-ACPD but had weak and variable effects on depressions induced by L-AP4. It had no effect on depressions induced by either (-)-baclofen or carbachol. In contrast, MAP4 (500 μM) reversed very effectively depressions induced by L-AP4 without affecting depressions induced by (1S,3S)-ACPD. MCCG (1mM) had the opposite activity; it antagonized depressions induced by (1S,3S)-ACPD but not those induced by L-AP4. Finally, (S)-4CPG (1 mM) reversed small depressions of field EPSPs induced by high concns. (50-100 μM) of (1S,3R)- and (1S,3S)-ACPD, but not L-AP4, while having no effect on large depressions induced by 10 μM (1S,3S)-ACPD in voltage-clamped cells. These results confirm and extend the effectiveness and selectivity of (+)-MCPG as an mGluR antagonist. The divergent effects of the group I antagonist, (S)-4CPG, can be explained by an indirect action on postsynaptic receptors which is manifest when high agonist concns. are used in non-voltage-clamp expts. The action of MCCG and MAP4 indicates that 2 pharmacol.-distinct mGluRs, belonging to classes II and III, can regulate synaptic transmission in the CA1 region via presynaptic mechanisms.
IT 157381-42-5, α-Methyl-L-AP 4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(group II and group III mGluRs involvement in presynaptic regulation of excitatory synaptic responses in hippocampus CA1 region)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 38 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:726787 HCAPLUS
DOCUMENT NUMBER: 123:160662
TITLE: Identification of 2-amino-2-methyl-4-phosphonobutanoic acid as an antagonist at the mGlu4a receptor
AUTHOR(S): Johansen, Patricia A.; Robinson, Michael B.
CORPORATE SOURCE: The Children's Seashore House, Children's Hospital of Philadelphia, Philadelphia, PA, 19104, USA
SOURCE: European Journal of Pharmacology, Molecular Pharmacology Section (1995), 290(2), R1-R3
CODEN: EJPPET; ISSN: 0922-4106
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 2-Amino-2-methyl-4-phosphonobutanoic acid (MAP4) was tested for interactions with the mGlu4a receptor which when expressed in baby hamster kidney (BHK570) cells couples to inhibition of forskolin-stimulated cAMP production MAP4 had no agonist activity at this receptor and caused a concentration-dependent inhibition of the reduction in forskolin-stimulated cAMP formation elicited by L-2-amino-4-phosphonobutanoic acid (L-AP4). Inhibition by MAP4 was consistent with a competitive mechanism of action (Schild slope = 1.2) with a Ki of 190 μM. MAP4 is the first antagonist identified for the mGlu4a receptor and should facilitate the determination of the physiol. role of the mGlu4a receptor.
IT 157381-42-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(identification of 2-amino-2-methyl-4-phosphonobutanoic acid as an antagonist at the mGlu4a receptor)
RN 157381-42-5 HCAPLUS
CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 39 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:465140 HCAPLUS
DOCUMENT NUMBER: 122:231442
TITLE: Antagonism of the synaptic depressant actions of L-AP4 in the lateral perforant path by MAP4
AUTHOR(S): Bushell, T. J.; Jane, D. E.; Tse, H.-W.; Watkins, J. C.; Davies, C. H.; Garthwaite, J.; Collingridge, G. L.
CORPORATE SOURCE: Dep. Anat., Univ. Bristol, Bristol, BS8 1TD, UK
SOURCE: Neuropharmacology (1995), 34(2), 239-41
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new mGluR antagonist, MAP4, the α-Me derivative of L-AP4 [(S)-2-amino-4-phosphonobutyrate], was found to antagonize the synaptic

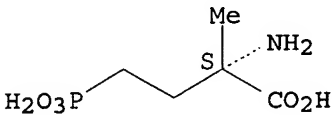
depressant actions of L-AP4 at the lateral perforant path synapse, in rat hippocampal slices.

IT 157381-42-5, α-Methyl-L-AP 4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antagonism of synaptic depressant actions of L-AP4 in lateral perforant path by MAP4)

RN 157381-42-5 HCAPLUS

CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 40 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:549540 HCAPLUS

DOCUMENT NUMBER: 121:149540

TITLE: Actions of two new antagonists showing selectivity for different sub-types of metabotropic glutamate receptor in the neonatal rat spinal cord

AUTHOR(S): Jane, D. E.; Jones, P. L. St. J.; Pook, P. C-K.; Tse, H-W.; Watkins, J. C.

CORPORATE SOURCE: Dep. Pharmacology, School Medical Sciences, Bristol, BS8 1TD, UK

SOURCE: British Journal of Pharmacology (1994), 112(3), 809-16
CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The presynaptic depressant action of L-2-amino-4-phosphonobutyrate (L-AP4) on the monosynaptic excitation of neonatal rat motoneurones has been differentiated from the similar effects produced by (1S,3R)-1-aminocyclopentane-1,3-dicarboxylate ((1S,3R)-ACPD), (1S,3S)-ACPD and (2S,3S,4S)-α-(carboxycyclopropyl)glycine (L-CCG-I), and from the postsynaptic motoneuronal depolarization produced by (1S,3R)-ACPD, by the actions of two new antagonists, α-methyl-L-AP4 (MAP4) and α-methyl-L-CCG-I (MCCG). Such selectivity was not seen with a previously reported antagonist, (+)-α-methyl-4-carboxyphenylglycine (MCPG). MAP4 selectively and competitively antagonized the depression of monosynaptic excitation produced by L-AP4 (KD 22 μM). At 10-fold higher concns., MAP4 also antagonized synaptic depression produced by L-CCG-I but in an apparently non-competitive manner. MAP4 was virtually without effect on depression produced by (1S,3R)- or (1S,3S)-ACPD. MCCG differentially antagonized the presynaptic depression produced by the range of agonists used. This antagonist had minimal effect on L-AP4-induced depression. The antagonism of the synaptic depression effected by (1S,3S)-ACPD and L-CCG-I was apparently competitive in each case but of varying effectiveness, with apparent KD values for the interaction between MCCG and the receptors activated by the two depressants calculated as 103 and 259 μM, resp. MCCG also antagonized the presynaptic depression produced by (1S,3R)-ACPD. Neither MAP4 nor MCCG (200-500 μM) affected motoneuronal depolarization produced by (1S,3R)-ACPD. At the same concns. the two antagonists produced only very weak and variable effects (slight antagonism or potentiation) on depolarizations produced by AMPA and NMDA. It is concluded that MAP4 is a potent and selective antagonist for these excitatory amino acid (EAA) receptors on neonatal rat primary afferent terminals that are preferentially activated by L-AP4, and that MCCG is a relatively selective

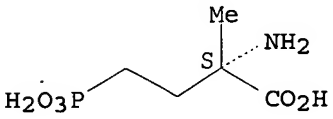
antagonist for different presynaptic EAA receptors that are preferentially activated by (1S,3S)-ACPD and (perhaps less selectively) by L-CCG-I. These receptors probably comprise two sub-types of metabotropic glutamate receptors neg. linked to adenylyl cyclase activity.

IT 157381-42-5, α-Methyl-L-AP4
RL: BIOL (Biological study)
(as selective antagonist of metabotropic glutamatergic receptor subtype of spinal cord of newborn)

RN 157381-42-5 HCAPLUS

CN L-Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L34 ANSWER 41 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:409939 HCAPLUS

DOCUMENT NUMBER: 121:9939

TITLE: Synthesis of α-methylhomocysteinethiolactone

AUTHOR(S): Haeusler, Johannes

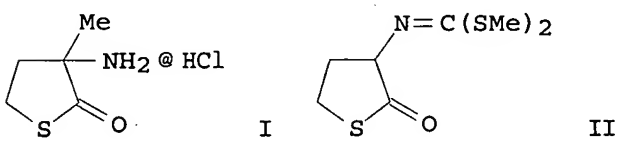
CORPORATE SOURCE: Inst. Org. Chem., Univ. Wien, Vienna, A-1090, Austria

SOURCE: Monatshefte fuer Chemie (1993), 124(10), 1071-5
CODEN: MOCMB7; ISSN: 0026-9247

DOCUMENT TYPE: Journal

LANGUAGE: German

GI



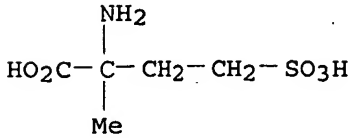
I II

AB A facile high yield large scale methylation procedure affording the racemic title compound (I) is reported utilizing the N-bis(methylthio)methylene-protected derivative II as an intermediate. The optical resolution of I is described leading to (S)-I. In addition I undergoes oxidative ring opening by bromine to HO3SCH2CH2CMe(NH2)CO2H.

IT 155330-54-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 155330-54-4 HCAPLUS

CN Isovaline, 4-sulfo- (9CI) (CA INDEX NAME)



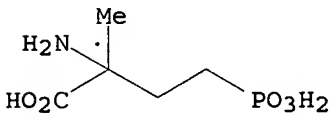
L34 ANSWER 42 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:584255 HCAPLUS
DOCUMENT NUMBER: 117:184255
TITLE: Structure-function relationships for analogs of L-2-amino-4-phosphonobutanoic acid on the quisqualic acid-sensitive AP4 receptor of the rat hippocampus
AUTHOR(S): Schulte, Marvin K.; Whittemore, Edward R.; Koerner, James F.; Johnson, Rodney L.
CORPORATE SOURCE: Med. Sch., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Brain Research (1992), 582(2), 291-8
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hippocampal CA1 pyramidal cell neurons are sensitized to depolarization by L-2-amino-4-phosphonobutanoic acid (L-AP4) following exposure to L-quisqualic acid (QUIS). The authors examined the interaction of 43 structural analogs of L-AP4 with both the 'induction' site and the QUIS-sensitive AP4 site in rat hippocampus. The synthesis of cis- and trans-4-phosphonoxy-L-proline, 3-(RS)-amino-5-phosphonopentanoic acid and 2(RS)-amino-5-phenyl-4(RS)-phosphonopentanoic acid (γ-benzyl AP4) are described. None of the test compds. interact with the induction site; thus L-QUIS remains the only compound known to induce this effect. However, one compound (L-2-amino-3-(5-tetrazolyl)-propanoic acid (L-aspartate tetrazole) 'pre-blocked' and reversed the effects of QUIS. In addition, the potency of 16 analogs increased more than 4-fold following exposure of slices to L-QUIS. Among these, L-AP4, L-AP5, 2-amino-4-(methylphosphino)butanoic acid (AMPB), and E-1(RS)-amino-3(RS)-phosphonocyclopentanecarboxylic acid (E-cyclopentyl AP4) displayed IC50 values of less than 0.100 mM after QUIS. The results presented here suggest that the QUIS-sensitive AP4 site requires a spatial configuration of functional groups similar to that present in E-cyclopentyl AP4. The presence of a primary amino group and a phosphorus-containing group (either monoanionic or dianionic) appear to be required, however, a carboxyl group is essential for interaction. The pharmacol. of the QUIS-sensitive AP4 site suggests that it is distinct from other known binding sites for L-AP4 in the central nervous system.

IT 78405-44-4
RL: BIOL (Biological study)
(quisqualic acid-sensitive AP4 receptor binding by, in CA1 hippocampus, structure in relation to)

RN 78405-44-4 HCAPLUS
CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



L34 ANSWER 43 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:506229 HCAPLUS
DOCUMENT NUMBER: 117:106229
TITLE: Herbicidal activity of phosphonic and phosphinic acid analogs of glutamic and aspartic acids
AUTHOR(S): Miliszkiewicz, Dorota; Wieczorek, Piotr; Lejczak, Barbara; Kowalik, Ewa; Kafarski, Pawel
CORPORATE SOURCE: Inst. Chem., Pedagog. Univ. Opole, Opole, 45-052, Pol.
SOURCE: Pesticide Science (1992), 34(4), 349-54
CODEN: PSSCBG; ISSN: 0031-613X
DOCUMENT TYPE: Journal
LANGUAGE: English

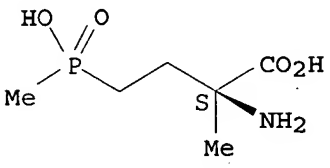
AB Phosphonic and phosphinic acid analogs of glutamic and aspartic acids were synthesized and screened for herbicidal activity on Lepidium sativum. Depending on the chemical structure, they exhibited significant or moderate herbicidal activity against L. sativum roots (with some representatives being equipotent with phosphinothricin), while their influence on shoot growth was negligible. Cucumis sativus appeared to be more tolerant to these analogs. The origin of this selectivity remains to be determined

IT 141609-98-5P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and herbicidal activity of)

RN 141609-98-5 HCAPLUS

CN L-Isovaline, 4-(hydroxymethylphosphinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 44 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:38443 HCAPLUS

DOCUMENT NUMBER: 114:38443

TITLE: Pyruvate analog adducts with NAD as lactate dehydrogenase inhibitors

INVENTOR(S): Cooper, Arthur J. L.

PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA

SOURCE: U.S., 8 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4950602	A	19900821	US 1987-16894	19870220 <--

PRIORITY APPLN. INFO.: US 1987-16894 19870220

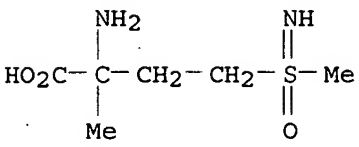
OTHER SOURCE(S): MARPAT 114:38443

AB Adducts of pyruvate and NAD+ adducts are lactate dehydrogenase inhibitors that can pass through the blood-brain barrier and are of use in the treatment of primary systemic lactic acidosis are prepared and characterized. A series of Na arylidene pyruvates were prepared and the adducts with NAD+ prepared by standard chemical These were then tested for inhibition of beef heart and rat brain lactate dehydrogenases. An NAD-pyruvate reduced the activity of the beef heart enzyme to 90% of control values and reduced the activity of the rat brain enzyme to 48% of controls in the presence of 0.24 mM pyruvate. An aldehyde analog was similarly active in the nanomolar range. Inhibition of lactate dehydrogenase activity in synaptosomes was also demonstrated.

IT 66735-67-9
RL: BIOL (Biological study)
(oxopentenoate from, reaction with NAD of, in preparation of lactate dehydrogenase inhibitor capable of passing blood-brain barrier, preparation of)

RN 66735-67-9 HCAPLUS

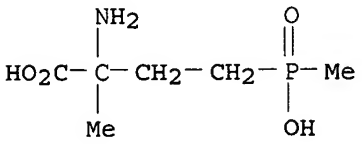
CN Isovaline, 4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



L34 ANSWER 45 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:32528 HCAPLUS
DOCUMENT NUMBER: 112:32528
TITLE: Inhibition of Escherichia coli glutamine synthetase by α- and γ-substituted phosphinothricins
AUTHOR(S): Logusch, Eugene W.; Walker, Daniel M.; McDonald, John F.; Franz, John E.; Villafranca, Joseph J.; DiIanni, Carolyn L.; Colanduoni, John A.; Li, Bin; Schineller, Jeffrey B.
CORPORATE SOURCE: Monsanto Agric. Co., St. Louis, MO, 63198, USA
SOURCE: Biochemistry (1990), 29(2), 366-72
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The inhibition of E. coli glutamine synthetase (GS) with α- and γ-substituted analogs of phosphinothricin [L-2-amino-4-(hydroxymethylphosphinyl)butanoic acid (PPT)], a naturally occurring inhibitor of GS, was investigated. These compds. displayed inhibition of bacterial GS that was competitive vs. L-glutamate, with Ki values in the low micromolar range. At concns. greater than Ki, the phosphinothricins caused time-dependent loss of enzyme activity, whereas dilution after enzyme inactivation resulted in recovery of enzyme activity. ATP was required for inactivation; the nonhydrolyzable ATP analog, AMP-PCP, failed to support inhibition of GS by the phosphinothricins. The binding of these inhibitors to the enzyme was also characterized by measurement of changes in protein fluorescence, which provided similar inactivation rate consts., k1 and k2, for the entire series of compds. Rate consts. (koff) for recovery were also determined by fluorescence measurement and were comparable for both PPT and the γ-hydroxylated analog, DL-γ-hydroxyphosphinothricin (GHPPT), and significantly greater for the α- and γ-alkyl-substituted compds. EPR spectra provided information on the interaction of the phosphinothricins with the Mn form of the enzyme in the absence of ATP, and significant binding was observed for PPT and GHPPT. 31P NMR expts. confirmed that enzyme inactivation was accompanied by hydrolysis of ATP, although phosphorylated phosphinothricins could not be detected in solution The kinetic behavior of these compds. was consistent with a mechanism involving inhibitor phosphorylation, followed by release from the active site and simultaneous hydrolysis to form phosphate and free inhibitor.

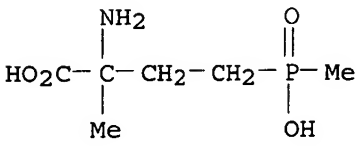
IT 115730-43-3
RL: BIOL (Biological study)
(glutamine synthetase of Escherichia coli inhibition by, kinetics and mechanism of)
RN 115730-43-3 HCAPLUS
CN Isovaline, 4-(hydroxymethylphosphinyl)-, monoammonium salt (9CI) (CA INDEX NAME)



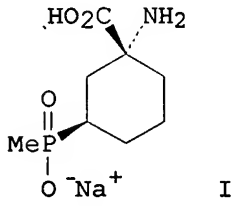
L34 ANSWER 46 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:150325 HCAPLUS
DOCUMENT NUMBER: 110:150325
TITLE: Substrate variability as a factor in enzyme inhibitor design: inhibition of ovine brain glutamine synthetase by α- and γ-substituted phosphinothricins
AUTHOR(S): Logusch, Eugene W.; Walker, Daniel M.; McDonald, John F.; Franz, John E.
CORPORATE SOURCE: Monsanto Agric. Co., Unit Monsanto Co., St. Louis, MO, 63198, USA
SOURCE: Biochemistry (1989), 28(7), 3043-51
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ovine brain glutamine synthetase (GS) utilizes various substituted glutamic acids as substrates. This information was used to design α- and γ-substituted analogs of phosphinothricin [L-2-amino-4-(hydroxymethylphosphinyl)butanoic acid, PPT], a naturally occurring inhibitor of GS. These compds. displayed competitive inhibition of GS, and a correlation between the inhibitor Ki values and the Km/Vmax values of the analogously substituted glutamates supports the hypothesis that the phosphinothricins participate in transition-state analog inhibition of GS. At concns. >Ki, these inhibitors caused biphasic time-dependent loss of enzyme activity, with initial pseudo-1st-order behavior; k'inact parameters were determined for several compds. and were similar to the 2.1 + 10-2 s-1 value measured for PPT. Dilution after GS inactivation caused a non-1st-order recovery of activity. Reactivation kinetics were insensitive to inhibitor and ADP concns. over wide ranges, although very high postdiln. concns. of inhibitor suppressed reactivation. The burst activity level, β, as well as the concentration of inhibitor required to suppress reactivation to this level, μ, expressed as a multiple of the Ki value, was characteristic for each compound in the phosphinothricin series. Increasing substitution of the phosphinothricin parent structure caused an increase in Ki values as well as in the inactivation/reactivation parameters. The kinetic behavior of these inhibitors was consistent with a mechanistic scheme involving initial phosphorylation and rapid partial inhibitor dissociation, followed by slow release of remaining bound inhibitor.

IT 115730-43-3
RL: BIOL (Biological study)
(glutamine synthetase of brain inhibition by, kinetics of, structure in relation to)
RN 115730-43-3 HCAPLUS
CN Isovaline, 4-(hydroxymethylphosphinyl)-, monoammonium salt (9CI) (CA INDEX NAME)

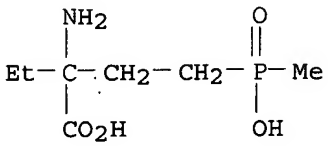


L34 ANSWER 47 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:510882 HCAPLUS
DOCUMENT NUMBER: 109:110882
TITLE: Synthesis of α- and γ-alkyl-substituted phosphinothricins: potent new inhibitors of glutamine synthetase
AUTHOR(S): Logusch, Eugene W.; Walker, Daniel M.; McDonald, John F.; Leo, Gregory C.; Franz, John E.
CORPORATE SOURCE: Monsanto Agric. Co., St. Louis, MO, 63167, USA
SOURCE: Journal of Organic Chemistry (1988), 53(17), 4069-74
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:110882
GI

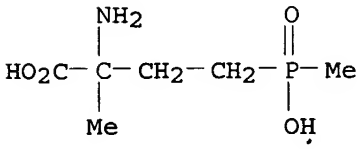


I

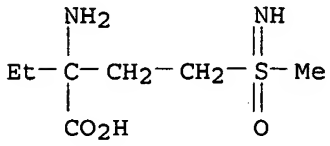
AB Considerations of substrate structural variability for the enzyme glutamine synthetase (GS, E.C. 6.3.1.2) have led to the design of α- and γ-substituted analogs of the naturally occurring GS inhibitor phosphinothricin (PPT). The novel cyclic inhibitor DL-cyclohexanephosphinothricin (I) was prepared via conjugate addition of MeP(OEt)2 to 2-cyclohexenone, followed by stereospecific Bucherer-Bergs amino acid synthesis. The stereochem. of I was determined by 2-dimensional NMR techniques. The substitute phosphinothricins function as active site probes useful for elucidating the mechanism of GS inhibition by PPT.
IT 115651-45-1P 115730-43-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and glutamine synthetase-inhibiting activity of)
RN 115651-45-1 HCAPLUS
CN Butanoic acid, 2-amino-2-ethyl-4-(hydroxymethylphosphinyl)-, monosodium salt (9CI) (CA INDEX NAME)



RN 115730-43-3 HCAPLUS
CN Isovaline, 4-(hydroxymethylphosphinyl)-, monoammonium salt (9CI) (CA INDEX NAME)

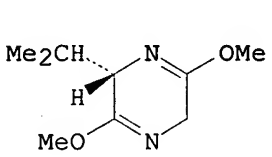


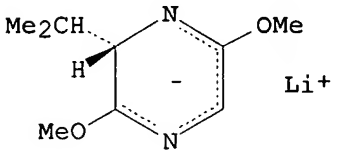
L34 ANSWER 48 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:132274 HCAPLUS
DOCUMENT NUMBER: 108:132274
TITLE: Amino acid sulfoximines: α-ethylmethionine sulfoximine
AUTHOR(S): Griffith, Owen W.
CORPORATE SOURCE: Med. Coll., Cornell Univ., New York, NY, 10021, USA
SOURCE: Methods in Enzymology (1987), 143(Sulfur Sulfur Amino Acids), 286-91
CODEN: MENZAU; ISSN: 0076-6879
DOCUMENT TYPE: Journal
LANGUAGE: English
AB α-Ethylmethionine sulfoxime, HO2CCEt(NH2)CH2CH2S(O)Me:NH, was prepared by treatment of HO2CCEt(NH2)CH2CH2SMe (I) with HCl. I was prepared by treatment of EtCOCH:CH2 with MeSH to give EtCOCH2CH2SMe which was converted to a hydantoin derivative with (NH4)2CO3 and NaCN and the product hydrolyzed to I.
IT 66735-68-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 66735-68-0 HCAPLUS
CN Butanoic acid, 2-amino-2-ethyl-4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



L34 ANSWER 49 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:5390 HCAPLUS

DOCUMENT NUMBER: 106:5390
TITLE: Asymmetric syntheses via heterocyclic intermediates. XXXII. Asymmetric synthesis of various non-proteinogenic amino acid methyl esters (functionalized in the carbon chain) and amino acids by the bislactim ether method
AUTHOR(S): Schoellkopf, Ulrich; Busse, Ulrich; Lonsky, Ralph; Hinrichs, Rolf
CORPORATE SOURCE: Inst. Org. Chem., Univ. Goettingen, Goettingen, D-3400, Fed. Rep. Ger.
SOURCE: Liebigs Annalen der Chemie (1986), (12), 2150-63
CODEN: LACHDL; ISSN: 0170-2041
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:5390
GI


I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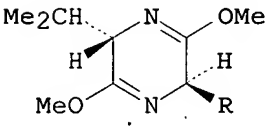
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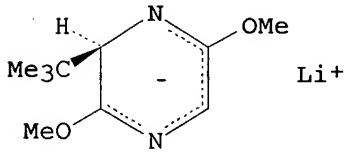
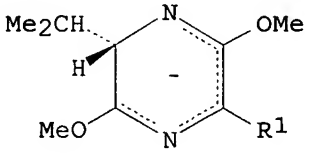
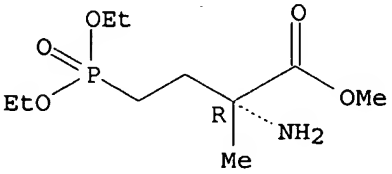

IV


V

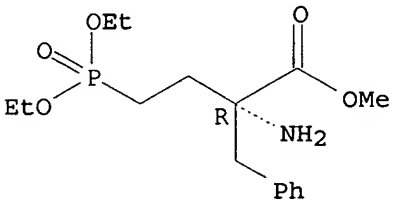
AB Bislactim ether I was treated with BuLi to give lithiated derivative II, which was alkylated with alkyl halides RX, e.g. BrCH2CH2P(O)(OEt)2, with a high degree of asym. induction to give alkylated ethers III, which can be hydrolyzed to give the corresponding optically active amino acid Me esters H2NCHRCO2Me. The asym. synthesis of amino acid Me esters was also achieved via the asym. alkylation of lithiated bislactim ethers IV and V (R1 = Me, CH2CH2PCO)(OEt)2].
IT 104739-07-3P 104739-19-7P 104739-20-0P
104739-21-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of, by bislactim ether method)
RN 104739-07-3 HCAPLUS
CN D-Isovaline, 4-(diethoxyphosphinyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



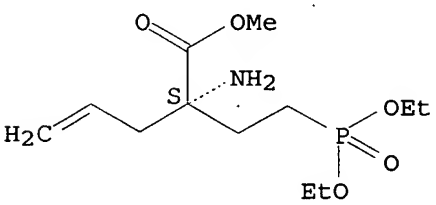
RN 104739-19-7 HCAPLUS
CN D-Phenylalanine, α-[2-(diethoxyphosphinyl)ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



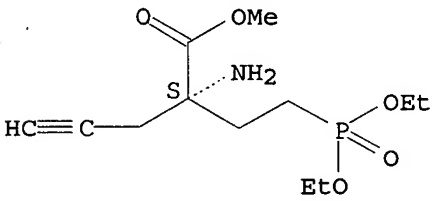
RN 104739-20-0 HCAPLUS
CN 4-Pentenoic acid, 2-amino-2-[2-(diethoxyphosphinyl)ethyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



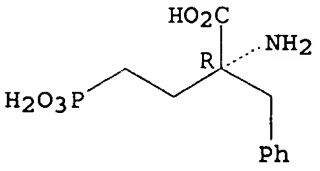
RN 104739-21-1 HCAPLUS
CN 4-Pentynoic acid, 2-amino-2-[2-(diethoxyphosphinyl)ethyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 104739-22-2P 104739-23-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 104739-22-2 HCAPLUS
CN D-Phenylalanine, α-(2-phosphonoethyl)- (9CI) (CA INDEX NAME)

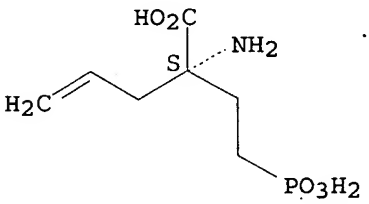
Absolute stereochemistry.



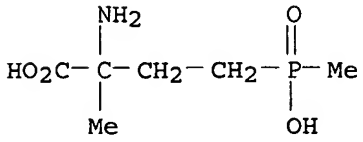
RN 104739-23-3 HCAPLUS
CN 4-Pentenoic acid, 2-amino-2-(2-phosphonoethyl)-, (S)- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.



L34 ANSWER 50 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:218953 HCAPLUS
DOCUMENT NUMBER: 104:218953
TITLE: Preliminary pharmacological investigation on 38 aminophosphonic acids and their derivatives
AUTHOR(S): Kleinrok, Zdzislaw; Kolasa, Krystyna; Chodkowska, Anna; Mastalerz, Przemyslaw; Kafarski, Pawel
CORPORATE SOURCE: Inst. Clin. Pathol., Med. Acad., Lublin, 20-090, Pol.
SOURCE: Polish Journal of Pharmacology and Pharmacy (1985), 37(5), 575-84
CODEN: PJPPAA; ISSN: 0301-0244
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Central pharmacol. properties of 38 aminophosphonic acids and their derivs., were investigated on mice and rats. Acute toxicity, neurotoxic activity and the influence on spontaneous locomotor activity, body temperature, electrogenic and pentetrazol convulsions and on the cerebral GABA [56-12-2] level were tested. The most active anticonvulsant compds. were (in a decreasing order of activity): 2-amino-7-phosphonoheptanoic acid [85797-13-3], 2-amino-5-phosphonovaleric acid [76726-92-6], 2-amino-8-phosphonooctanoic acid [98517-63-6], 2-amino-2-methyl-3-methylphosphonopropionic acid [73870-67-4], and 3-amino-3-hydroxy-5-phosphonovaleric acid acid [99305-89-2]. Some structure-activity relations are discussed.
IT 65482-86-2
RL: BIOL (Biological study)
(central pharmacol. properties of)
RN 65482-86-2 HCAPLUS
CN Isovaline, 4-(hydroxymethylphosphinyl)- (9CI) (CA INDEX NAME)



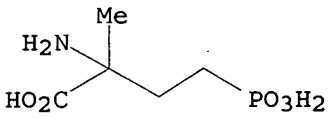
L34 ANSWER 51 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:198188 HCAPLUS
DOCUMENT NUMBER: 102:198188
TITLE: Antagonist activity of methyl-substituted analogs of 2-amino-4-phosphonobutanoic acid in the hippocampal slice
AUTHOR(S): Crooks, Stephen L.; Freund, Ronald K.; Halsrud, David A.; Koerner, James F.; Johnson, Rodney L.
CORPORATE SOURCE: Coll. Pharm., Univ. Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Brain Research (1985), 329(1-2), 346-9
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Four monomethyl-substituted analogs of 2-amino-4-phosphonobutanoic acid (APB) [23052-81-5] an antagonist of excitatory pathways in the central nervous system, were prepared to investigate the steric requirements of the APB receptor. Me groups were incorporated at the amino, α-, β-, and γ-positions. The β- [95742-06-6] and γ-methyl-substituted analog [79469-40-2] of APB were moderately potent antagonists in excitatory synapses to the hippocampal perforant path, as judged by extracellular recording techniques, whereas the N- [96249-46-6] and α-methyl-substituted analog [78405-44-4] had much lower potencies. All of these APB analogs had very low potencies in the Schaffer collateral pathway. The APB receptors in the perforant path displayed more tolerance of methyl-substitution at the β- and γ-positions of APB than at the amino or α-positions in this system.

IT 78405-44-4
RL: BIOL (Biological study)
(hippocampus synaptic neurotransmission inhibition by, mol. structure in relation to)

RN 78405-44-4 HCAPLUS
CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



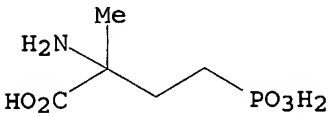
L34 ANSWER 52 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:197823 HCAPLUS
DOCUMENT NUMBER: 102:197823
TITLE: Displacement of DL-[3H]-2-amino-4-phosphonobutanoic acid ([3H]APB) binding with methyl-substituted APB analogs and glutamate agonists
AUTHOR(S): Robinson, Michael B.; Crooks, Stephen L.; Johnson, Rodney L.; Koerner, James F.
CORPORATE SOURCE: Med. Sch., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Biochemistry (1985), 24(10), 2401-5
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The binding of DL-2-amino-4-phosphonobutanoic acid (I) [20263-07-4] to rat brain synaptic membranes was saturable (Kd = 6.0 μM; Bmax = 380 pmol/mg/protein), Ca2+- and Cl--dependent, and diminished upon freezing the membrane preparation The L-isomer of I [23052-81-5], L-glutamic acid [56-86-0], and L-aspartic acid [56-84-8] were more potent as displacers of I binding than the resp. D-isomers. With the exception of kynurenic acid [492-27-3], all the other compds. examined (L- and D-glutamic acid [6893-26-1], L-glutamate tetrazole [65914-80-9], D-2-amino-5-phosphonopentanoic acid [79055-68-8], 2(RS)-amino-2-methyl-4-phosphonobutenoic acid [78405-44-4], DL-2-amino-4-(methylphosphino)butenoic acid [53369-07-6], 2(RS)-amino-3(RS)-methyl-4-phosphonobutanoic acid [95742-06-6], and 2(RS)-amino-4(RS)-phosphonopentanoic acid [79469-40-2]) were more potent as displacers of I binding than as inhibitors of synaptic transmission in the lateral perforant path; however, the L-isomer of I was equipotent in both assays. The ligand specificity in binding to the I site is discussed in relation

to the regulation of the lateral perforant pathway and the pharmacol. of glutamate receptors.

IT 78405-44-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(aminophosphonobutanoate binding to brain response to)

RN 78405-44-4 HCAPLUS
CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)



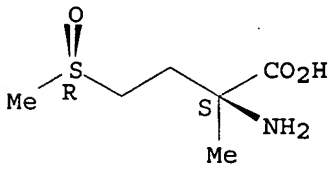
L34 ANSWER 53 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:178450 HCAPLUS
DOCUMENT NUMBER: 102:178450
TITLE: Gas chromatographic separation of enantiomeric sulfur compounds on Chirasil-Val
AUTHOR(S): Bayer, Ernst; Kuesters, Ernst; Nicholson, Graeme J.; Frank, Hartmut
CORPORATE SOURCE: Inst. Org. Chem., Univ. Tuebingen, Tuebingen, D-7400/1, Fed. Rep. Ger.
SOURCE: Journal of Chromatography (1985), 320(2), 393-6
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The gas chromatog. separation of sulfoxide antipodes, including aliphatic sulfoxides, on quartz fused silica capillaries coated with the chiral silicone phase Chirasil-Val is reported. The compds. were esterified before anal. A flame ionization detector and H carrier gas were used.

IT 95833-63-9 95833-64-0 95833-65-1
95833-66-2 95833-67-3 95833-68-4
RL: ANST (Analytical study); PROC (Process)
(separation of, by gas chromatog. on Chirasil-Val)

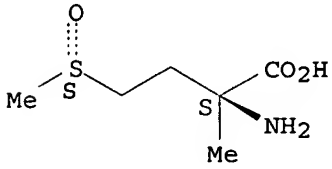
RN 95833-63-9 HCAPLUS
CN L-Isovaline, 4-(methylsulfinyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



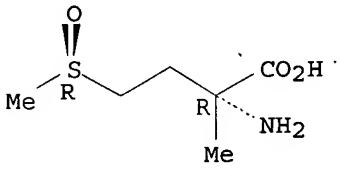
RN 95833-64-0 HCAPLUS
CN L-Isovaline, 4-(methylsulfinyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



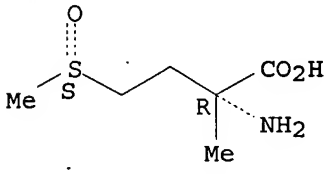
RN 95833-65-1 HCAPLUS
CN D-Isovaline, 4-(methylsulfinyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



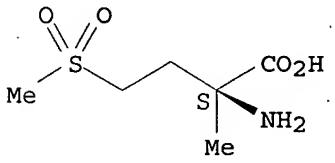
RN 95833-66-2 HCAPLUS
CN D-Isovaline, 4-(methylsulfinyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



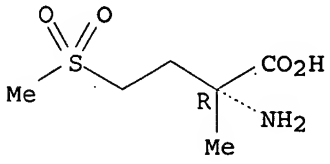
RN 95833-67-3 HCAPLUS
CN L-Isovaline, 4-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



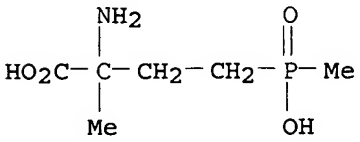
RN 95833-68-4 HCAPLUS
CN D-Isovaline, 4-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

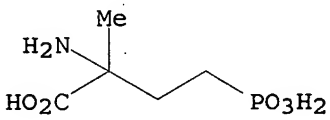


L34 ANSWER 54 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:457044 HCAPLUS
DOCUMENT NUMBER: 95:57044
TITLE: Inhibition of rat liver glutamine synthetase by phosphonic analogs of glutamic acid
AUTHOR(S): Lejczak, B.; Starzemska, H.; Mastalerz, P.
CORPORATE SOURCE: Inst. Org. Phys. Chem., Tech. Univ., Wroclaw, PL-50370, Pol.
SOURCE: Experientia (1981), 37(5), 461-2
CODEN: EXPEAM; ISSN: 0014-4754

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Analogs of glutamic acid, α-methylglutamic acid, and glutamine in which the α- or γ-COOH groups are replaced by PO3H2 or P(O)(OH3)OH groups competitively inhibit rat liver glutamine synthetase. The Ki values are comparable to or lower than Km for L-glutamate.
IT 65482-86-2 78405-44-4
RL: BIOL (Biological study)
(glutamine synthetase inhibition by)
RN 65482-86-2 HCAPLUS
CN Isovaline, 4-(hydroxymethylphosphinyl)- (9CI) (CA INDEX NAME)



RN 78405-44-4 HCAPLUS
CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

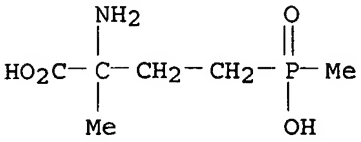


L34 ANSWER 55 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:151895 HCAPLUS
DOCUMENT NUMBER: 94:151895
TITLE: Herbicide for controlling numerous monocotyl and dicotyl, annual and perennial weeds
INVENTOR(S): Rupp, Walter; Finke, Manfred; Bieringer, Hermann; Langelueddeke, Peter; Kleiner, Hans Jerg
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Patentschrift (Switz.), 6 pp.
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

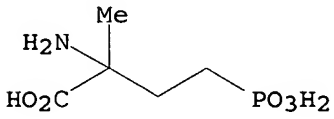
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 620812	A5	19801231	CH 1976-7118	19760604 <--
PRIORITY APPLN. INFO.:			CH 1976-7118 A	19760604

AB The phosphinates R3COCR4(NH2)(CH2)2P(O)R1R2.(HY)m (R1 = alkyl; R2 and R3 = OH, SH, alkoxy, cycloalkoxy, alkenyloxy, Ph, NH2, alkylamino, etc.; R4 = H or alkyl; Y = anion, m = 0-1) are herbicides. Thus, in pot expts., postemergence [1-(3-amino-3-carboxy)propyl]methylphosphinic acid-HCl [59542-49-3] (2.5 kg/ha) totally controlled Sinapis, Chenopodium, Matricaria, Stellaria, and other weeds. The synthesis of the compds. is given.
IT 65482-86-2P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and herbicidal activity of)
RN 65482-86-2 HCAPLUS

CN Isovaline, 4-(hydroxymethylphosphinyl)- (9CI) (CA INDEX NAME)

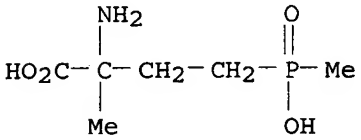


L34 ANSWER 56 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:140 HCAPLUS
DOCUMENT NUMBER: 94:140
TITLE: Cytostatic activity in vitro of cycloleucine, aspartic acid and glutamic acid phosphonic analogs
AUTHOR(S): Dus, Danuta; Salwa, Jan; Mastalerz, Przemyslaw
CORPORATE SOURCE: Inst. Immunol. Exp. Therapy, Polish Acad. Sci., Wroclaw, Pol.
SOURCE: Archivum Immunologiae et Therapiae Experimentalis (1980), 28(3), 433-8
CODEN: AITEAT; ISSN: 0004-069X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cytostatic activity of 18 new phosphonic acid derivative of cycloleucine, aspartic acid, and glutamic acid was tested against human KB and mouse L1210s leukemia cell lines in vitro. Four of the tested compds. revealed their cytostatic activity at 10 μg/mL.
IT 78405-44-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cytostatic activity of)
RN 78405-44-4 HCAPLUS
CN Isovaline, 4-phosphono- (9CI) (CA INDEX NAME)

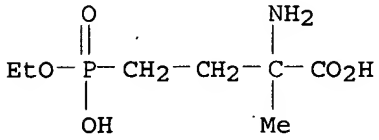


L34 ANSWER 57 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:408479 HCAPLUS
DOCUMENT NUMBER: 93:8479
TITLE: Phosphonic analogs of α-methylaspartic and α-methylglutamic acids
AUTHOR(S): Gruszecka, Ewa; Soroka, Miroslaw; Mastalerz, Przemyslaw
CORPORATE SOURCE: Inst. Org. Phys. Chem., Polytech. Univ., Wroclaw, 50370, Pol.
SOURCE: Polish Journal of Chemistry (1979), 53(11), 2327-31
CODEN: PJCHDQ; ISSN: 0137-5083
DOCUMENT TYPE: Journal
LANGUAGE: English
AB MeC(NH2)(CO2H)(CH2)nP(O)(OH)R (I; R = Me, OEt; n = 1, 2) were prepared by the Strecker reaction of MeCO(CH2)nP(O)(OEt)R, followed by hydrolysis. MeCOCH2CH2CO2Me was treated with R1PH(O)(OEt) (II, R1 = OH, Me) and then hydrolyzed to give R1P(O)(OH)CMe(NH2)CH2CH2CO2H, whereas H2NCMe:CHCO2Et was treated with II and then hydrolyzed to give R1P(O)(OH)CMe(NH2)CH2CO2H. I (R = Me, n = 1) and II (R1 = OH) at 100 μg/mL inhibited the growth of

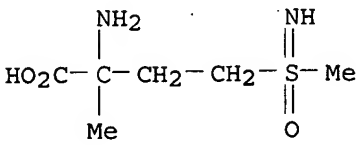
L1210 s1 cells by 50%.
IT 65482-86-2P 73870-66-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 65482-86-2 HCAPLUS
CN Isovaline, 4-(hydroxymethylphosphinyl)- (9CI) (CA INDEX NAME)



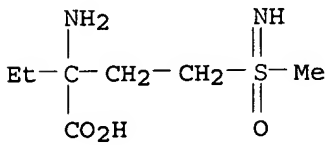
RN 73870-66-3 HCAPLUS
CN Isovaline, 4-(ethoxyhydroxyphosphinyl)- (9CI) (CA INDEX NAME)



L34 ANSWER 58 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:198299 HCAPLUS
DOCUMENT NUMBER: 90:198299
TITLE: Inhibition of glutathione biosynthesis by prothionine sulfoximine (S-n-propyl homocysteine sulfoximine), a selective inhibitor of γ-glutamylcysteine synthetase
AUTHOR(S): Griffith, Owen W.; Anderson, Mary E.; Meister, Alton
CORPORATE SOURCE: Med. Coll., Cornell Univ., New York, NY, USA
SOURCE: Journal of Biological Chemistry (1979), 254(4), 1205-10
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB DL-Prothionine SR-sulfoximine [70085-86-8] and α-methyl-DL-prothionine-SR-sulfoximine [70056-05-2] were prepared and found to markedly inhibit γ-glutamylcysteine synthetase [9023-64-7] but to not significantly affect glutamine synthetase [9023-70-5]. After injection of prothionine sulfoximine into mice, the level of kidney glutathione [70-18-8] decreased rapidly to .apprx.20% of the control level indicating that a large fraction, rather than a small pool, of glutathione participates in rapid turnover. The rapid decline of the glutathione level that occurs after inhibition of glutathione synthesis reflects the normal rate of intracellular glutathione utilization by the γ-glutamyl cycle. A number of related sulfoximines were synthesized and tested as inhibitors of glutamine and γ-glutamylcysteine synthetases.
IT 66735-67-9 66735-68-0
RL: PRP (Properties)
(glutamylcysteine synthetase inhibition by)
RN 66735-67-9 HCAPLUS
CN Isovaline, 4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



RN 66735-68-0 HCAPLUS
CN Butanoic acid, 2-amino-2-ethyl-4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



L34 ANSWER 59 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:541899 HCAPLUS
DOCUMENT NUMBER: 89:141899
TITLE: Herbicidal compositions containing phosphinic acid derivatives
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Belg., 23 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 854753	A1	19771117	BE 1977-177677	19770517 <--
NL 7705259	A	19771121	NL 1977-5259	19770512 <--
NL 179866	B	19860701		
NL 179866	C	19861201		
DD 130094	A5	19780308	DD 1977-198900	19770512 <--
ZA 7702828	A	19780426	ZA 1977-2828	19770512 <--
JP 52139727	A	19771121	JP 1977-55550	19770516 <--
JP 57026564	B	19820605		
BR 7703155	A	19780131	BR 1977-3155	19770516 <--
AU 7725151	A	19781123	AU 1977-25151	19770516 <--
US 4168963	A	19790925	US 1977-797171	19770516 <--
AT 7703474	A	19800115	AT 1977-3474	19770516 <--
AT 358315	B	19800910		
DK 142441	B	19801103	DK 1977-2129	19770516 <--
DK 142441	C	19810810		
IL 52098	A	19810227	IL 1977-52098	19770516 <--
CS 207456	B2	19810731	CS 1977-3206	19770516 <--
HU 27812	A2	19831128	HU 1977-HO1982	19770516 <--
HU 185003	B	19841128		
SE 7705872	A	19771118	SE 1977-5872	19770517 <--
SE 439416	B	19850617		
SE 439416	C	19850926		
FR 2351598	A1	19771216	FR 1977-15031	19770517 <--
FR 2351598	B1	19840217		
SU 659069	A3	19790425	SU 1977-2480278	19770517 <--
GB 1587292	A	19810401	GB 1977-27063	19770517 <--

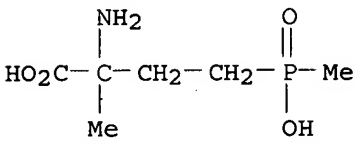
PRIORITY APPLN. INFO.: CH 1976-6153 A 19760517
AB Herbicidal compns. contain the phosphinic acid derivs.

R3COR5(NHR4)CH2CH2P(:X)R1R2.m(HY) (R1 = mono-, di-, and trihalomethyl; R2 = OH, SH, OMe, or SMe, Me = mineral or organic base; R3 = R2 or C1-12 alkoxy, C3-8 cycloalkoxy, PhO, piperidine, etc.; R4 = H, C1-4 acyl, etc.; R5 = H or C1-4 alkyl; X = O or S; Y = mineral or organic anion; m = 0, 1/2 or 1). Thus, the herbicidal effect was demonstrated by (3-amino-3-carboxypropyl)methylphosphonic acid.HCl [59542-49-3] without injury to crop plants. The synthesis of the phosphinates is given.

IT 65482-86-2P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and herbicidal activity of)

RN 65482-86-2 HCAPLUS

CN Isovaline, 4-(hydroxymethylphosphinyl)- (9CI) (CA INDEX NAME)



L34 ANSWER 60 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:500916 HCAPLUS

DOCUMENT NUMBER: 89:100916

TITLE: Differential inhibition of glutamine and γ-glutamylcysteine synthetases by α-alkyl analogs of methionine sulfoximine that induce convulsions

AUTHOR(S): Griffith, Owen W.; Meister, Alton

CORPORATE SOURCE: Dep. Biochem., Cornell Univ. Med. Coll., New York, NY, USA

SOURCE: Journal of Biological Chemistry (1978), 253(7), 2333-8
CODEN: JBCHA3; ISSN: 0021-9258

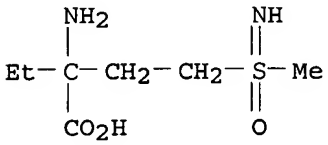
DOCUMENT TYPE: Journal

LANGUAGE: English

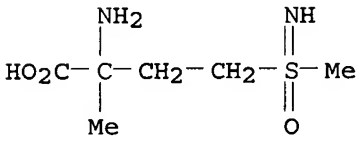
AB α-Methyl-DL-methionine (SR)-sulfoximine [66735-67-9] and α-ethyl-DL-methionine (SR)-sulfoximine [66735-68-0], like L-methionine (SR)-sulfoximine [15985-39-4], induced convulsions in mice and inhibited glutamine synthetase [9023-70-5] irreversibly; α-ethylmethionine sulfoximine was .apprx.50% as inhibitory as methionine sulfoximine and α-methylmethionine sulfoximine. However, whereas α-methylmethionine sulfoximine and methionine sulfoximine inhibited γ-glutamylcysteine synthetase [9023-64-7] markedly, α-ethylmethionine sulfoximine did not, nor did administration of the α-Et analog produce the decrease in tissue glutathione [70-18-8] levels found after giving methionine sulfoximine or its α-Me analog. The α-alkyl methionine sulfoximine analogs cannot be catabolized via the corresponding α-keto or α-imino acids, and, like other α-substituted amino acids, are probably not metabolized to a significant extent in vivo; this suggests that the amino acid sulfoximine mols. themselves, rather than their metabolites, are directly involved in the induction of convulsions. Possible explanations for the reported lack of correlation between the occurrence of convulsions and the levels of glutamine synthetase activity (and its substrates and product) are considered.

IT 66735-68-0
RL: PRP (Properties)
(glutamine synthetase and glutamylcysteine synthetase inhibition by, convulsions in relation to)

RN 66735-68-0 HCAPLUS
CN Butanoic acid, 2-amino-2-ethyl-4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



IT 66735-67-9P
RL: PREP (Preparation)
(preparation and glutamine synthetase and glutamylcysteine synthetase inhibition by)
RN 66735-67-9 HCAPLUS
CN Isovaline, 4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



L34 ANSWER 61 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:70494 HCAPLUS
DOCUMENT NUMBER: 88:70494
TITLE: Herbicidal composition
INVENTOR(S): Rupp, Walter; Finke, Manfred; Bieringer, Hermann; Langelueddeke, Peter
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 22 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2717440	A1	19771201	DE 1977-2717440	19770420 <--
DE 2717440	C2	19840405		
NL 7705259	A	19771121	NL 1977-5259	19770512 <--
NL 179866	B	19860701		
NL 179866	C	19861201		
DD 130094	A5	19780308	DD 1977-198900	19770512 <--
ZA 7702828	A	19780426	ZA 1977-2828	19770512 <--
JP 52139727	A	19771121	JP 1977-55550	19770516 <--
JP 57026564	B	19820605		
BR 7703155	A	19780131	BR 1977-3155	19770516 <--
AU 7725151	A	19781123	AU 1977-25151	19770516 <--
US 4168963	A	19790925	US 1977-797171	19770516 <--
AT 7703474	A	19800115	AT 1977-3474	19770516 <--
AT 358315	B	19800910		
DK 142441	B	19801103	DK 1977-2129	19770516 <--
DK 142441	C	19810810		
IL 52098	A	19810227	IL 1977-52098	19770516 <--
CS 207456	B2	19810731	CS 1977-3206	19770516 <--
HU 27812	A2	19831128	HU 1977-HO1982	19770516 <--

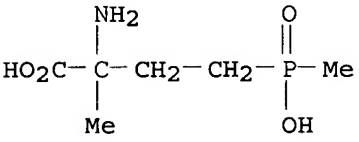
HU 185003	B	19841128			
SE 7705872	A	19771118	SE 1977-5872		19770517 <--
SE 439416	B	19850617			
SE 439416	C	19850926			
FR 2351598	A1	19771216	FR 1977-15031		19770517 <--
FR 2351598	B1	19840217			
SU 659069	A3	19790425	SU 1977-2480278		19770517 <--
GB 1587292	A	19810401	GB 1977-27063		19770517 <--
PRIORITY APPLN. INFO.:			CH 1976-6153	A	19760517

AB The methylphosphinic acid derivs. R3C(O)CR5(NHR4) (CH2)2 P(:X)R1R2.(HY)m (R1 = Me or halomethyl; R2 = OH, ONa, etc; R3 = OH, OEt, NH2, etc; R4 = H, acyl, etc; R5 = H or alkyl; X = O or S; Y = anion, m = 0, 1/2, or 1) are herbicides. Thus, postemergence application of 2.5 kg 3-amino-3-carboxypropylmethylphosphinic acid [51276-47-2]/ha totally controlled weeds such as Sinapis, Matricaria, Stelloria, etc., in pot expts. The synthesis of the compds. is given.

IT 65482-86-2P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and herbicidal activity of)

RN 65482-86-2 HCAPLUS

CN Isovaline, 4-(hydroxymethylphosphinyl)- (9CI) (CA INDEX NAME)



L34 ANSWER 62 OF 62 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1956:73727 HCAPLUS
DOCUMENT NUMBER:	50:73727
ORIGINAL REFERENCE NO.:	50:13802g-i,13803a-i,13804a-g
TITLE:	Sulfur-containing amino acids
AUTHOR(S):	Reisner, David B.
CORPORATE SOURCE:	Wallace & Tiernan, Inc., Newark, NJ
SOURCE:	Journal of the American Chemical Society (1956), 78, 2132-5 CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE:	Journal
LANGUAGE:	Unavailable
OTHER SOURCE(S):	CASREACT 50:73727

GI For diagram(s), see printed CA Issue.

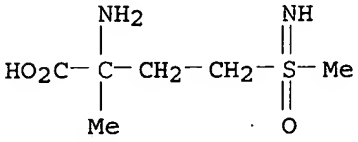
AB MeCH:CHCHO (140 g.) and 96 g. MeSH in the presence of 2 drops of piperidine stirred 0.5 hr. at 5-10° and 3 hrs. at room temperature, the mixture treated with an addnl. 28 g. MeSH, heated about 1 hr. at 90°, diluted with 500 cc. Et2O, washed with dilute HCl and H2O, dried, and evaporated, and the residue distilled gave 201 g. MeSCHMeCH2CHO (I), b23 80°. AcCH:CH2 (27 g.) and 18 g. MeSH yielded 35.4 g. Ac(CH2)2SMe, b55 106°, nD25 1.4711. I (48.5 g.), 113 g. (NH4)3SO3, 25.5 g. NaCN, 335 cc. EtOH, and 335 cc. H2O heated 5 hrs. with stirring at 55°, the mixture concentrated to about 300 cc., treated cautiously with 50 cc. concentrated HCl, heated 7 min. at about 90°, refrigerated, and filtered, and the residue washed with 200 cc. H2O yielded 49 g. 5-(β-benzylmercapto)propylhydantoin, m. 117-18°(from EtOAc). Similarly were prepared the following compds. RR'C.CO.NH.CO.NH (R, R', m.p., and % yield given): MeS(CH2)2, Me, 109.5-10.5°, 93.8; MeSCHMeCH2, H, 191-2°, 50.1; MeSCHPhCH2, H, 173-4°, 491.
S-Benzyl-4-methylhomocysteine (7.17 g.), m. 222.5-3.5° (decomposition)

(from H2O) (obtained in 94% yield from the hydantoin) (0.69,0.74, 0.93) (the figures given in parentheses through out this abstract represent the Rf values of the resp. compds. obtained by ascending paper chromatography with BuOH-AcOH, lutidine-collidine, and PhOH-H2O, resp.) in 300 cc. liquid NH3 treated with about 1.7 g. Na, the solution decolorized with about 1 g. NH4Cl, treated with 5 cc. MeI, and evaporated, the residue treated with 125 cc. H2O, washed with Et2O, filtered, neutralized with concentrated HCl to pH about 6, concentrated to about 50 cc., diluted with 50 cc. Me2CO, and refrigerated, and the crystalline deposit recrystd. from aqueous MeOH yielded 4.1 g. MeSCHMeCH2CH(NH2)CO2H (II), m. 236-7° (decomposition), (0.44, 0.53, 0.79). Similarly were prepared: MeS(CH2)2CMe(NH2)CO2H, 61%, m. 284-5° (decomposition) (from aqueous MeOH), (0.45, 0.50, 0.77); MeSCHPh(CH2)2CH(NH2)CO2H, 49.3%, m. 201-2° (decomposition) (from H2O). BzCH2SMe (21.8 g.) in 50 cc. dry Et2O added with stirring to 1.4 g. LiAlH4 in 10 cc. dry Et2O, the mixture refluxed 1 hr. with stirring, cooled, and treated with stirring with 200 cc. ice water and 100 cc. 5N H2SO4, the aqueous layer washed with Et2O, the combined Et2O solns. washed, dried, and evaporated under a jet of dry air, and the residue distilled gave 18.4 g. MeSCH2CH(OH)Ph (III), b1.8 113-14.5°. III (170 mg.) treated with MeI yielded III. MeI, m. 134-5° (decomposition). III (15.8 g.) in 25 cc. dry CHCl3 treated with cooling with 9.2 g. SOCl2 in 15 cc. dry CHCl3, the mixture cooled 0.5 hr., kept at room temperature overnight and evaporated, the residue heated gently with 5 cc. dry CHCl3 and 5 cc. SOCl2, and the mixture distilled gave 14.3 g. MeSCH2CHClPh (IV), b2.8 106-7°, nD25 1.5692. AcNHCH(CO2Et)2 (11.6 g.) and 200 mg. KI added with stirring to 1.23 g. Na in 100 cc. absolute EtOH, the mixture treated with 10 g. IV in 1 portion, stirred 2 hrs. at room temperature, refluxed 5 hrs., and filtered hot, the residue washed with about 50 cc. hot EtOH, the combined alc. solns. evaporated to dryness in vacuo, the residual oil kept at room temperature overnight, and the crystalline material washed with dilute HCl and H2O and dried in vacuo over KOH pellets yielded 16 g. MeSCH2CHPhC(NHAc)(CO2Et)2 (V), m. 95-6° (from Et2O-pentane). Crude V (14.4 g.), 40 cc. H2O, and 10 cc. concentrated HCl refluxed 6 hrs. with stirring, the mixture treated with 40 cc. H2O and 10 cc. concentrated HCl, refluxed 1.5 hrs. with stirring, cooled to room temperature, the solid refluxed 8 hrs. with stirring with 80 cc. glacial AcOH and 10 cc. concentrated HCl, treated with Norit, and filtered, the residue washed with H2O, the combined filtrates evaporated in vacuo, the residue (about 10 g.) triturated with 50 cc. Me2CO and filtered, and the residue washed with Me2CO and dried yielded 5 g. MeSCH2CHPhCH(NH2)CO2H.HCl (VI.HCl), m. 208-9° (decomposition); the Me2CO solns. combined and evaporated to dryness, the residue refluxed 6.5 hrs. with 25 cc. H2O, 25 cc. glacial AcOH, and 10 cc. concentrated HCl, the solution evaporated to dryness in vacuo, the residue washed with Me2CO and neutralized with AmNH2, and a 1-g. portion dissolved in 8 cc. H2O and neutralized with AmNH2 to pH 6, diluted with 25 cc. Me2CO, and filtered, and the residue washed with 15 cc. Me2CO yielded 300 mg. VI; the filtrate diluted with Me2CO gave a 2nd crop, 350 mg. MeSH (14 g.) passed with stirring and cooling into 1.2 g. Na in 150 cc. absolute MeOH, the mixture treated with stirring and cooling with 50 g. Me α-benzamidosenecioate, diluted with 200 cc. absolute MeOH and 200 cc. dry C6H6, stirred 1 hr. at room temperature, allowed to stand overnight, treated with 3.12 g. glacial AcOH, and evaporated to dryness in vacuo at room temperature, the residue washed with warm dry C6H6, the C6H6 evaporated, the residue (58 g.), 300 cc. 85% HCO2H, 300 cc. concentrated HCl, and 300 cc. H2O refluxed 6 hrs., the solution concentrated to about 50 cc., washed with Et2O, neutralized with AmNH2 to pH 6, diluted with 350 cc. Me2CO, and refrigerated 2 days, and the white crystals washed with 300 cc. Me2CO and 200 cc. Et2O yielded 16.8 g. S-methylpenicillamine, m. 281-2° (0.38, 0.50, 0.80); it was also obtained in the same manner from 2-phenyl-4-isopropylidene-5-oxazolone and 30 g. MeSH. MeSH (16 g.) passed into 1.2 g. Na in 300 cc. absolute MeOH, the solution treated with cooling and stirring with 62.3 g. 2-phenyl-4-benzal-5-oxazolone in 500 cc. warm, dry C6H6, the mixture stirred about 1 hr., kept at room temperature, treated with 3.12 g. glacial AcOH, and evaporated to dryness in vacuo, the residue treated with 100 cc. warm C6H6 and filtered, the

filtrate diluted with 100 cc. warm C6H6 and 500 cc. pentane, and chilled, and the deposit washed with 150 cc. pentane yielded 74 g. PhCH(SMe)CH(NHBz)CO2Me (VII), m. 97-8.5° (from EtOAc-pentane). Crude VII (32.9 g.) hydrolyzed with 150 cc. H2O, 150 cc. concentrated HCl, and 150 cc. 90% HCO2H, the solution concentrated in vacuo to near dryness, and the precipitate washed with three 100-cc. portions H2O, dissolved in 75 cc. H2O, neutralized to pH 6 with AmNH2, and chilled yielded 12.5 g. S-methyl-3-phenylcysteine, m. 178-9° (decomposition) (0.51, 0.65, 0.88). The following sulfoxides were prepared by oxidation of the appropriate sulfides with H2O2 by the method of Toennies and Kolb (C.A. 33, 5359.9) (% yield, m.p., and Rf values given): PhCH2S(O)CHMeCH2CH(NH2)CO2H, 64.7, 214-15° (decomposition) (from H2O), (0.45, 0.60, 0.92); MeS(O)CH2CH2CMe(NH2)CO2H, 91.8, 239.5-40.5° (decomposition) (from aqueous MeOH), (0.14, 0.35, 0.77); MeS(O)CHMeCH2CH(NH2)CO2H (VIII), 84.4, 213.5-14.5° (from aqueous MeOH), (0.13, 0.40, 0.80); MeS(O)CH2CHPhCH(NH2)CO2H, 74.4, 205-6° (decomposition) (from aqueous MeOH), (0.33, 0.59, 0.87); MeS(O)CHPhCH2CH(NH2)CO2H, 87.7, 189-90° (decomposition) (from aqueous MeOH), (0.33, 0.47, 0.85); Me2CHCH[S(O)Me]CH(NH2)CO2H, 77.7, 166-7° (from aqueous MeOH), (0.14, 0.40, 0.76); PhCH[S(O)Me]CH(NH2)CO2H, 73.2, 147-8° (decomposition) (from aqueous MeOH), (0.29, 0.54, 0.82). VIII (600 mg.), 3 cc. H2O, 2 cc. MeOH, 0.2 cc. concentrated HCl, and 2 cc. 30% H2O2 refluxed 2 hrs., treated with 1 cc. 30% H2O2, refluxed again 2 hrs., neutralized with AmNH2 to pH 6.5, diluted with 100 cc. Me2CO and filtered, and the residue washed with 50 cc. Me2CO yielded 550 mg. MeS(O2)CHMeCH2CH(NH2)CO2H, m. 230-1° (decomposition) (from aqueous MeOH), (0.14, 0.50, 0.72). In the same manner was prepared PhCH2S(O2)CH2CH2CH(NH2)CO2H, 70.6%, m. 229-30° (decomposition) (from H2O), (0.50, 0.65, 0.84). The following sulfones were prepared by the oxidation on the appropriate sulfides with H2O2 in the presence of NH4 molybdate and HClO4 by the method of Toennies and Kolb (C.A. 35, 6571.1) (% yield, m.p., and Rf values given): MeS(O2)CH2CH2CMe(NH2)CO2H, 73.6, 288-9° (decomposition) (from aqueous MeOH), (0.16, 0.45, 0.65); MeS(O2)CH2CHPhCH(NH2)CO2H (IX), 50.8, 222-3° (decomposition) (from H2O), (0.32, 0.61, 0.79); MeS(O2)CHPhCH2CH(NH2)CO2H (X), 95.4, 196.5-7.5° (decomposition), (0.37, 0.55, 0.79); Me2CHCH[S(O2)Me]CH(NH2)CO2H, 77.7, 166-7° (from aqueous MeOH), (0.14, 0.53, 0.68); MeS(O2)CHPhCH(NH2)CO2H, 51.2, 141-2° (decomposition) (from aqueous MeOH), (0.30, 0.52, 0.70). VIII (6.0 g.) treated dropwise with stirring at 3° with 10.4 cc. concentrated H2SO4, the mixture heated with stirring to 45°, treated during 1 hr. at 48° with 54 cc. 1.4N HN3 in CHCl3, then heated with stirring 5 hrs. at 48°, treated with 13.5 cc. HN3 solution, heated 5 hrs. with stirring at 50°, stirred overnight at room temperature, poured with stirring onto 75 g. crushed ice, neutralized with solid Ba(OH)2 to about pH 2.5 then to pH 5 with solid BaCO3, and centrifuged, the supernatant decanted, the residue mixed with H2O, centrifuged, and decanted, this operation repeated until free of amino acid, the combined aqueous solns. concentrated in vacuo at 50° to about 100 cc., treated with C, and filtered, and the filtrate concentrated to about 40 cc., filtered, and evaporated to dryness yielded 6.4 g. MeS(:NH)CHMeCH2CH(NH2)CO2H, m. 199-200° (decomposition) (from aqueous MeOH), (0.08, 0.38, 0.71). In the same manner was prepared: MeS(:NH)CH2CH2CHMe(NH2)CO2H,100, 199-200° (decomposition) (from aqueous MeOH), (0.10, 0.35, 0.67). IX (100 mg.) treated with about 60 mg. N-bromosuccinimide gave MeS(O2)CH2CHPhCHO, isolated as the 2,4-dinitrophenylhydrazone, m. 188-9° (decomposition). X gave similarly MeS(O2)CHPhCH2CHO, isolated as the 2,4-dinitrophenylhydrazone, decomposed at 196-8° with a change from yellow to red at 169°. Only 4 of the amino acids suppressed the multiplication of T2 bacteriophage of Escherichia coli strain A.T.C.C. number 11303 at pH 7 and 37° at 100 p.p.m. or less.

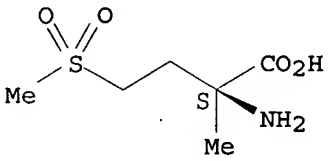
IT 66735-67-9P, Sulfoximine, 3-amino-3-carboxybutyl methyl
95833-67-3P, Isovaline, 4-(methylsulfonyl)- 911673-23-9P
, Isovaline, 4-(methylsulfinyl)-

RL: PREP (Preparation)
(preparation of)
RN 66735-67-9 HCAPLUS
CN Isovaline, 4-(S-methylsulfonimidoyl)- (9CI) (CA INDEX NAME)



RN 95833-67-3 HCAPLUS
CN L-Isovaline, 4-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 911673-23-9 HCAPLUS
CN Isovaline, 4-(methylsulfinyl)- (5CI) (CA INDEX NAME)